

Enumeration of mast cells in the human umbilical cord: implications for coiling patterns

A. I. Alsamawi¹, S. A. H. Al-Sharqi¹, H. J. Mubarak²

¹College of science, Mustansiriyah University, Baghdad, Iraq

²Medical College, Al-Nahrain University, Baghdad, Iraq

The abnormal umbilical cord coiling pattern affects the well-being of the newborn in different ways. Moreover the differentiation of mast cell according to these patterns may also varies.

The objective: to investigate the detection and enumeration of mast cells in different patterns in human coiling cords in order to explore their effect on the newborn baby health.

Materials and methods. Umbilical cord samples were collected from 105 healthy pregnant women. The cords were collected immediately after labor and kept in formalin (10%), according to coil type. Three major categories of umbilical cord coiling (normocoiled, hypercoiled, and hypocoiled) were determined according to the Umbilical Cord Index (UCI). The histological sections of the umbilical cord were collected according to UCI. This step is followed by using different histological stains, including hematoxylin and eosin and toluidine blue stains. The expression of the CD117 mast cell population in the umbilical cord tissue was determined using the immunohistochemical method in the subamniotic, perivascular and central areas. The enumeration of mast cells was done by direct counting and using Image J software.

Results. The comparison of mast cell counts using Image J showed statistically significant variations ($P < 0.05$) between normocoiled and hypercoiled cords in mast cell populations. No significant changes ($P > 0.05$) were found in mast cell counts between normocoiled and hypocoiled umbilical cords.

Conclusions. The mast cell distribution interpretation suggested that mechanical coiling during embryonic growth affects mast cell dispersal in sectioned umbilical cords. This interpretation's functional relevance should be applied to coiling events that do not have harmful outcomes on the fetus.

Future research could be done on the distribution of mast cells in the abnormally coiled umbilical cords associated with negative perinatal outcomes.

Keywords: coiling index, mast cell, umbilical cord.

Тучні клітини у пуповині людини: вплив на характер звивистості

A. I. Alsamawi, S. A. H. Al-Sharqi, H. J. Mubarak

Аномалії звивистості пуповини по-різному впливають на стан новонародженого. Диференціювання тучних клітин у пуповині відповідно до видів її звивистості також може бути різним.

Мета дослідження: виявлення та підрахунок тучних клітин у пуповині різної звивистості та вивчення їхнього впливу на стан новонароджених.

Матеріали та методи. Зразки пуповин були зібрані у 105 здорових вагітних. Пуповини збирали відразу після пологів і зберігали у формаліні (10%) відповідно до типу звивистості. За даними індексу звивистості пуповини (ІЗП) розрізняли три типи її звивистості – нормальний тип, гіперзвивиста та гіпозвивиста пуповина.

Гістологічні зрізи пуповини були зібрані відповідно до ІЗП. Цей етап виконано за допомогою використання різних гістологічних барвників, включаючи гематоксилін та еозин і толудіновий синій. Експресію популяції тучних клітин CD117 у тканині пуповини визначали за допомогою імуногістохімічного методу у субамніотичній, периваскулярній та центральній ділянках. Кількість тучних клітин визначали шляхом прямого підрахунку з використанням програмного забезпечення Image J.

Результати. Порівняння кількості тучних клітин за допомогою Image J продемонструвало статистично значущу відмінність ($P < 0,05$) у їхній кількості між пуповинами з нормальним типом звивистості та гіперзвивистими пуповинами. Не було встановлено значущої відмінності ($P > 0,05$) у кількості тучних клітин між пуповинами з нормальною звивистістю та гіпозвивистими пуповинами.

Висновки. Інтерпретація розподілу тучних клітин засвідчила, що механічна звивистість пуповини під час ембріонального росту впливає на дисперсію цих клітин у перерізаній пуповині. Функціональна значущість цієї інтерпретації повинна застосовуватися до типів звивистості, які не зумовлюють шкідливих наслідків для плода.

У майбутньому можуть бути проведені дослідження розподілу тучних клітин в аномально звивистих пуповинах, пов'язаних із негативними перинатальними результатами.

Ключові слова: індекс звивистості пуповини, тучні клітини, пуповина.

Aristotle, a renowned Greek philosopher from ancient times (384–322 BC), initially characterized the umbilical cord as the link between the developing fetus and its mother [1]. The human umbilical cord is essential for the development, well-being, and ability to survive of the fetus. Nevertheless, the perinatal period can be influenced by various variables, includ-

ing kinking, compressions, traction, and torsion. The embryonic architecture vessels are particularly vulnerable [2].

There are around forty helical umbilical coils. Conversely, deviations in the umbilical cord length might result in negative consequences, including irregular development, complications during childbirth, and, ultimately, fetal demise [3].

Mast cells originate from hematopoietic precursor cells. They can differentiate into mast cell progenitors in bone marrow and human umbilical cord blood, as demonstrated in laboratory settings [4]. Mast cells are acknowledged for participating in inflammatory reactions and their correlation with allergies and immunological ailments [5]. The regulation of mast cell development, maturation, and expansion is inherently governed by the activity of a specific kind of receptor tyrosine kinase known as KIT (CD117), belonging to class III. The protein in question is synthesized by encoding the protooncogene *c-kit*, and it is noteworthy that mast cells are the sole cell type that exhibits a high level of expression for this particular protein [6].

The umbilical cord vessels differ in function and histological structure; they consist of two arteries and one vein. The arteries transport the oxygen-depleted blood and waste materials from the baby toward the placenta. In contrast, the umbilical vein transports the rich in oxygen and nutrition blood in the opposite direction (from the placenta towards the fetus) [7]. Throughout the early stages of embryonic development, when the gestation process occurs, the amniotic sac will form and appear at the beginning of the second week, forming layers that enlarge into a thin membrane called the amnion. This vital structure is established in the eighth week of gestation [8].

The superficial subamnioblastic zone is covered by amnioblast cells; the Wharton zone, which is located between the subamniotic region and the blood vessels; the perivascular zone, which surrounds the vessels, and the intervascular zone, which is located between the three vessels of the human cord, are the four central regions that are typically taken into account in most reports [9]. One of the most prominent physical characteristics of the umbilical cord is its helical twist. Screening for abnormalities in the degree of umbilical cord coiling is a straightforward process associated with many unfavorable birth outcomes, such as premature birth [10].

The phenomenon of cord coiling has been hypothesized to arise from hemodynamic stress or external influences during fetal development, including nuchal cords, fetal movement, and variations in umbilical vascular growth rates, muscle fiber morphology, or genetic factors [11]. The fetus has sufficient space for movement and growth due to the amniotic cavity's expansion and the umbilical cords elongation. Wharton's jelly plays a vital role in protecting the umbilical vessels during the prenatal period, allowing the fetus to move and rotate freely without disrupting its blood flow [12, 13].

The coiling characteristic of the umbilical cord was first documented by Jacobus Berengarius in 1521. It is characterized by completing an entire 360-degree spiral trajectory of an umbilical vessel around Wharton's jelly [2]. UCI is a quantitative measure that characterizes the degree of coiling in the umbilical cord. It is calculated by dividing the number of twists in the cord by its length, expressed in centimeters [14, 15]. The average umbilical cord index at birth has been determined to be 0.17 ± 0.009 twists/cm. It has been established that the umbilical cord index within the range of 0.07 to 0.30 twists/cm indicates appropriate umbilical cord coiling [16]. As per the classification provided by UCI, umbilical cords can be categorized into three groups based on their coiling characteristics: hypocoiled (UCI < 10th percentile), normocoiled (UCI

between the 10th and 90th percentile), and hypercoiled (UCI > 90th percentile) [17, 18].

The objective: is to objectively investigate the detection and enumeration of mast cells in different patterns in human coiling cords in order to explore their effect on the newborn baby health.

MATERIALS AND METHODS

This study was conducted at Department of Obstetrics and Gynecology in Al-Kadhimiya Educational Hospital in Baghdad during the period from January 2023 to June 2023 the study samples were collected from 105 healthy pregnant women; the umbilical cord samples were collected immediately after the labor process and kept in formalin (10%) for histological and immunohistochemical study, according to the coil type of the cord. The total number of samples was 105; the samples were divided equally into three major categories (35 samples of normocoiled, 35 samples of hypercoiled, and 35 samples of hypocoiled). Determining the umbilical cord coiling index necessitates considering two fundamental principles pertaining to the dimensions of the umbilical cord. This measurement should be conducted promptly following the birth of the neonate.

The first principle involves the measurement of the umbilical cord's length, which can be accomplished using a steel measuring tape.

The second principle quantifies the number of coils within the umbilical cord [14, 15]. The umbilical cord coiling index can easily be estimated by dividing the total number of coils by the total length of the umbilical cord as the equation below:

$$UCI = (\text{Number of coils}) / (\text{Length of umbilical cord in Centimeters})$$

Tissue samples from umbilical cord after delivery were prepared for histopathological studies according to Suvarna Kim and her colleagues method [19]. The tissue samples first stained with Hematoxylin and Eosin stained then an Immunohistochemically staining was carried out after formalin had been fixed.

Paraffin embedded tissue blocks were cut at 5µm thick section. All sections deparaffinized in xylene, then decreasing grades of ethanol and incubated with phosphate buffered saline. The steps of staining protocol with monoclonal antibodies toward CD117 from (Gemened, Biotechnologies, Inc.) as follows:

- Step 1: endogenous peroxidase blocking
- Step 2: primary antibody incubation
- Step 3: poly HRP conjugate incubation
- Step 4: substrate / chromogen
- Step 5: counterstaining
- Step 6: Mounting

The intensity of positive staining with the CD117 mast cell was graded as:

1. Negative 0: <25% of mast cells showed positive staining.
2. Mild (+1): 25-50% of mast cells showed positive staining.
3. Moderate (+2): 50-75% of cells showed positive staining.
4. Strong (+3): >75% of cells showed positive staining.

The use of Toluidine Blue solution is frequently observed in metachromatic staining, a process that is distinctive for cationic or basic dyes. The effectiveness of this staining technique is influenced by several factors, including the pH level, concentration of the dye, and temperature. Metachromatic

staining is commonly observed in mast cells, cartilage, cylindrical cells, and mucopolysaccharides, particularly those with a high number of sulphate groups. Following the application of toluidine blue dye, mast cells in the umbilical cord were evaluated using two distinct ways.

The first method involved directly counting mast cells in all three regions of the umbilical cord tissue (namely the subamniotic region, perivascular region, and the central region located between the two arteries and the vein) using a Olympus light compound microscope, Japan, in an objective manner.

The second method utilized (Image J) software for analysis the accurate count of mast cell. All participants agreed to provide the investigator with the specimens.

The ethics committee of College of Science, Mustansiriyah University approved this work. Additionally, the article costs were borne by the author and his colleagues themselves with no external funding sources. The obtained data were subjected to analysis of variance (ANOVA) test to compare the means of various groups with each other. Results were expressed in descriptive analysis. LSD test was used to calculate the significant differences between tested means.

The indication of no significant differences between tested mean ($P \leq 0.05$) was considered statically significant while values of ($P \geq 0.05$) were considered statistically nonsignificant. The statistical analysis was carried out by SPSS version 20.

RESULTS AND DISCUSSION

The mast cells in the connective tissues are classified according to the composition of intracellular secretory granules [20] and are contributing to tissue repair [21–23]. Mast

cells progenitor cells expressing cluster of differentiation molecule 34 (CD34) in bone marrow and then migrate into the circulation as CD34 and CD117 labeled progenitors that could penetrate into the tissues and then differentiate into a functional tissue-specific mast cells under the influence of various cytokines [24]. It was reported that mast cells are occasionally seen in the connective tissue of the umbilical cords, in addition to fibroblast – like cells [25].

The topography of mast cells was described to be more massively found around the umbilical vessels, however, the number of mast cells in the human umbilical cord was not definitely reported. In this study, the topographic distribution and density of mast cells regarding the correlation with coiling index were the goals to reveal the mast cells functions in the normal and abnormal coiled cord. The mast cells could not be clearly examined in the cord sections stained with hematoxylin and eosin, the immunohistochemical CD117 labeling enabled enhanced visualization of these cells, a result that was supported by previous articles [6].

The normocoiled cords involved in this study showed considerable assembly at the perivascular connective tissue, figure 1, moreover the peripheral connective tissue (deeper to the subamniotic layering) showed also fair number of mast cells which was subjectively to a lesser comparable number than the perivascular regions, figure 2. While the sectioned hypercoiled cord showed greater assembly of mast cells at the subamniotic layering and the central core regions of the sectioned cord as shown in figure 3.

The hypocoiled cords showed subjective uniformity of mast cells distribution in both the subamniotic and pe-

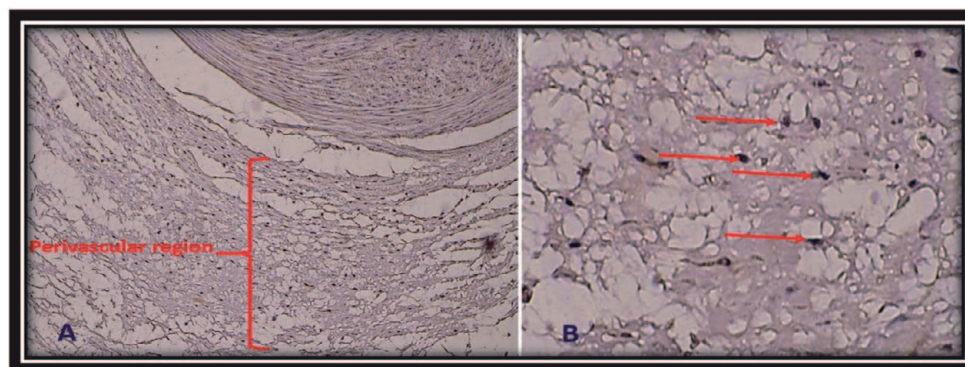


Fig. 1. Mast cell distribution in perivascular region of umbilical cord (H&E) A.(X4), B.(X10)

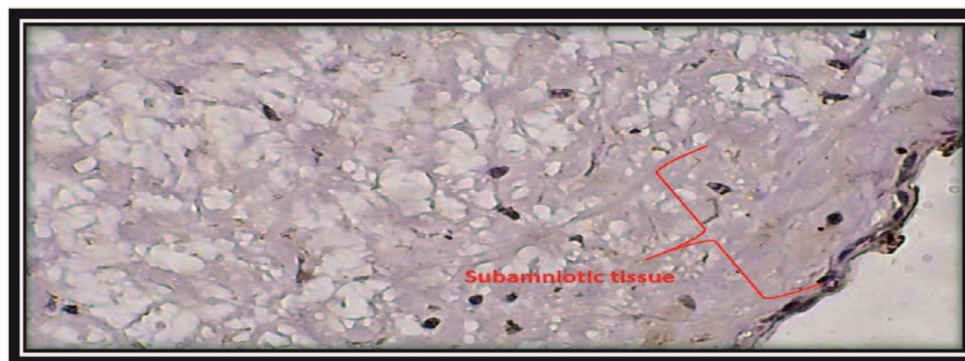


Fig. 2. Mast cell in subamniotic tissue of umbilical cord (H&E) (X4)

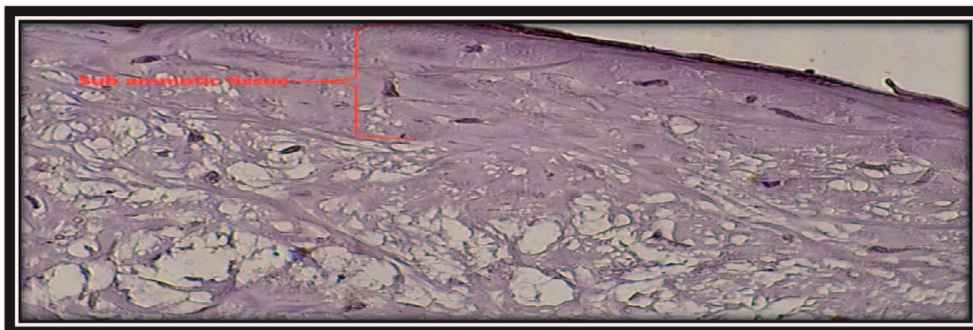


Fig. 3. Cross section in hypercoiling umbilical cord labelled with CD117 showed the subamniotic mast cell (H&E) (X4)

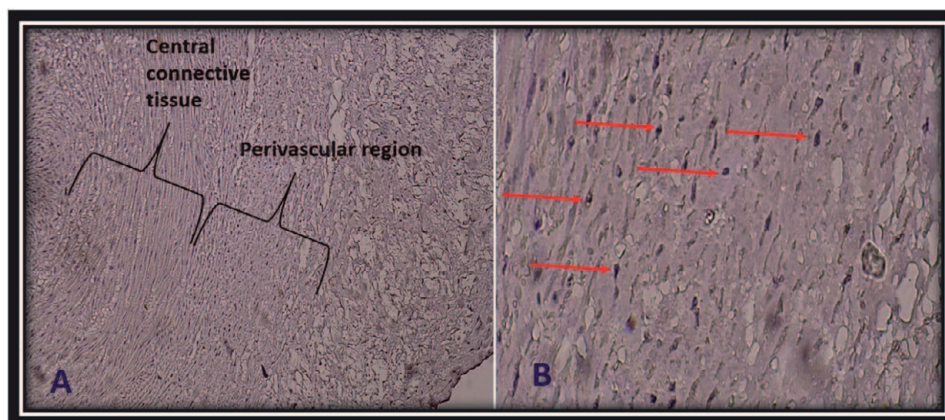


Fig. 4. Cross section in hypocoiling umbilical cord showed the prevalence of mast cells in the perivascular & central region (H&E) A. (X4), B. (X10)

ripheral connective tissue, that were less in assembly compared to the perivascular and central connective tissues of these cords as it indicates in figure 4.

The subjective evaluation of CD117 labeled mast cells allocation may suggest that the mast cells migrate from the umbilical vessels in the normocoiled cord and thus assembled around these vessels and in the peripheral connective tissues to the outside of these vessels. It seems that hypercoiling may introduce mechanical compression on the umbilical vessels and thus impeding extravasation of mast cells and deviating the precoiling extravasated mast cells to the subamniotic and central connective tissues.

The mechanical laxity associated with hypocoiling maintained extravasation of mast cells that aggregate in all parts of these cord with greater number adjacent to the vessels compared to the periphery.

Therefore, the above interpretation of mast cells distribution suggested that the distribution of mast cells in the sectioned umbilical cords involved in this study is affected by the mechanical influence of coiling occurring during embryonic development. According to the criteria of sample collection in this study, the functional significance of this interpretation should be applied for the coiling phenomena that do not have harmful sequels on the fetus.

Future researches could be done on the distribution of mast cells in the abnormally coiled umbilical cords associated with bad perinatal outcome. A comprehensive histological analysis was conducted on umbilical cord tis-

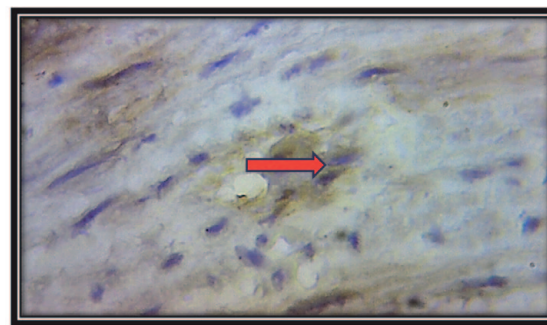


Fig.5. Cross section in Umbilical cord showed mast cells (arrowheads) with granules in cytoplasmic (X40)

sue samples representing normocoiling, hypercoiling, and hypocoiling patterns. This analysis involved the usage of an immunohistochemical technique to facilitate the detection of the cellular population (CD 117 mast cell) in umbilical cord tissue as shown in figure 5.

The intensity of CD117 mast cell expression in umbilical cord tissue of the three coiling cord types (Normocoiled, Hypercoiled, and Hypocoiled) in three critical regions of the umbilical cord sections, namely the subamniotic region, perivascular region, and the central region located between the two arteries and the vein, were observed in the figure 6 and also in tables 1, 2 and 3 below.

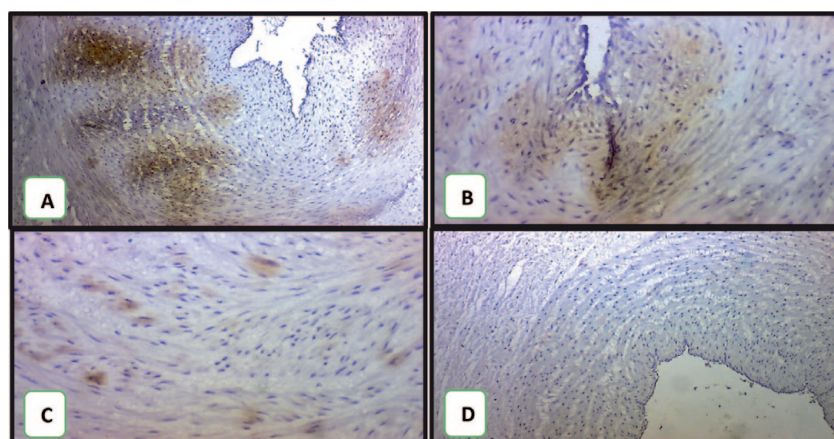


Fig. 6. Immunohistochemical staining method detection of CD117 mast cells in the Umbilical cord showed: (A) Strong (+3) positive cytoplasmic expression. (B) Moderate (+2) positive cytoplasmic expression (C) Mild (+1) positive cytoplasmic expression (D) Negative (0) expression (A&D, X4-B&C, X10)

Table 1

Intensity of CD117 mast cell expression in umbilical cord tissue of normocoiled

Grade / Intensity of CD117	Subamniotic region No. (%)	Perivascular region No. (%)	Center region No. (%)
0	16 (45.71)	0 (0)	0 (0)
+1	19 (54.28)	9 (25.71)	15 (42.85)
+2	0 (0)	15 (42.85)	12 (34.28)
+3	0 (0)	11 (31.42)	8 (22.85)
Total	35	35	35

Results are expressed as a percentage.

Table 2

Intensity of CD117 mast cell expression in umbilical cord tissue of hypocoiled

Grade / Intensity of CD117	Subamniotic region	Perivascular region	Center region
0	27 (77.14)	0 (0)	0 (0)
+1	8 (22.85)	4 (11.42)	23 (65.71)
+2	0 (0)	20 (57.14)	12 (34.28)
+3	0 (0)	11 (31.42)	0 (0)
Total	35	35	35

Results are expressed as a percentage.

Table 3

Intensity of CD117 mast cell expression in umbilical cord tissue of hypercoiled

Grade / Intensity of CD117	Subamniotic region	Perivascular region	Center region
0	4 (11.42)	8 (22.85)	12 (34.28)
+1	21 (60)	27 (77.14)	23 (65.71)
+2	4 (11.42)	0 (0)	0 (0)
+3	6 (17.14)	0 (0)	0 (0)
Total	35	35	35

Results are expressed as a percentage.

Table 4

Enumeration of mast cells in Normocoiled and Hypercoiled umbilical cord

Mast cell count		
Statistic	Normal	Hyper
Number of samples	35	35
Mean	27.5	20.7
Std. Error of Mean	1.827	1.832
Median	27.5	19.5
Std. Deviation	5.77	5.79
Minimum	19	13
Maximum	35	31
P value	0.05	

Table 5

Enumeration of mast cells in Normocoiled and Hypocoiled umbilical cord

Mast cell count		
Statistic	Normal	Hypo
Number of samples	35	35
Mean	27.5	24.5
Std. Error of Mean	1.827	1.002
Median	27.5	25
Std. Deviation	5.77	3.17
Minimum	19	19
Maximum	35	29
P value	NSIG	

Correspondingly, this analysis involved the application of a specialized toluidine blue stain to facilitate the identification and enumeration of mast cells in the three coiling types of the umbilical cord. The enumeration was done using the (Image J) software as a second and conformation technique for the previous work done using the CD117. The comparative analysis of mast cell counting using (Image J) in all three umbilical cord types revealed that there was a significant difference ($P < 0.05$) in mast cell numbers between the normocoiled and hypercoiled cords as it shown in table 4, Nevertheless, there were no significant difference ($P > 0.05$) in mast cell numbers in the comparison showed between the normocoiled and hypocoiled umbilical cord as shown in table 5.

CONCLUSIONS

The interpretation of mast cells distribution suggested that the dispersal of mast cells in the sectioned umbilical cords involved in this study is affected by the mechanical influence of coiling occurring during embryonic development. According to the criteria of sample collection in this study, the functional significance of this interpretation should be applied for the coiling phenomena that do not have harmful sequels on the fetus.

Future researches could be done on the distribution of mast cells in the abnormally coiled umbilical cords associated with bad perinatal outcome.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper. All authors concur that no financial, personal, or professional affiliations could be construed as influencing the research presented.

Information about the authors

- Alsamawi Ali Ibrahim** – Lecturer Assistance, Biology Department, College of Science, Mustansiriyah University, Iraq. *E-mail: samawi79@uomustansiriyah.edu.iq*
ORCID: 0000-0001-8296-5233
- Al-Sharqi Sahar Abdul Hadi** – Professor, Dr. Biology Department, College of Science, Mustansiriyah University, Iraq. *E-mail: saharalsharqi@uomustansiriyah.edu.iq*
ORCID: 0000-0002-4727-6413
- Mubarak Hydar Jawad** – Professor, Dr. Dean Assistance, College of Medicine, Al-Nahrain University, Iraq. *E-mail: hayder_67_67@nahrainuniv.edu.iq*
ORCID: 0000-0002-3127-4915

Відомості про авторів

- Алсамаві Алі Ібрагім** – асистент лектора, кафедра біології, Науковий коледж, Університет Мустансірія, Ірак. *E-mail: samawi79@uomustansiriyah.edu.iq*
ORCID: 0000-0001-8296-5233.
- Аль-Шаркі Сахар Абдул Хаді** – проф., д-р біол. наук, Науковий коледж, Університет Мустансірія, Ірак. *E-mail: saharalsharqi@uomustansiriyah.edu.iq*
ORCID: 0000-0002-4727-6413
- Мубарак Гідар Джавад** – проф., д-р, помічник декана, Медичний коледж, Університет Аль-Нахрейн, Ірак. *E-mail: hayder_67_67@nahrainuniv.edu.iq*
ORCID: 0000-0002-3127-4915

REFERENCES

- Gill RW, Kossoff G, Warren PS, Garrett WJ. Umbilical venous flow in normal and complicated pregnancy. *Ultrasound Med Biol.* 1984;10(3):349-63. doi: 10.1016/0301-5629(84)90169-8.
- Gupta S, Faridi MMA, Krishnan J. Umbilical Coiling Index. *J Obstet Gynecol India.* 2006;56(4):315-19.
- Biradar A, Shreedevi K, Neelamma P, Mudanur SR. Umbilical coiling index and its association with perinatal mortality and morbidity in a low resource tertiary care hospital of northern Karnataka – a prospective observational study. *New Ind J OBGYN.* 2020;7(1):10-5.
- Elieh Ali Komi D, Wöhrl S, Bielory L. Mast Cell Biology at Molecular Level: a Comprehensive Review. *Clin Rev Allergy Immunol.* 2020;58(3):342-65. doi: 10.1007/s12016-019-08769-2.
- Woźniak E, Owczarczyk-Saczonek A, Lange M, Czarny J, Wygonowska E, Placek W, et al. The Role of Mast Cells in the Induction and Maintenance of Inflammation in Selected Skin Diseases. *Int J Mol Sci.* 2023;24(8):7021. doi: 10.3390/ijms24087021.
- Mazreah SA, Shahsavari M, Kalati PA, Mazreah HA. Immunohistochemical evaluation of CD117 in mast cell of aggressive periodontitis. *J Indian Soc Periodontol.* 2020;24(3):216-20. doi: 10.4103/jisp.jisp.243.19.
- Ebbing C, Kessler J, Moser D, Rasmussen S. Single umbilical artery and risk of congenital malformation: population-based study in Norway. *Ultrasound Obstet Gynecol.* 2020;55(4):510-5. doi: 10.1002/uog.20359.
- Schoenwolf Gary C, Bleyl Steve B, Brauer Philip R, Philippa H. Francis-West. Second week: becoming bilaminar and fully implanting. In: *Larsen's human embryology.* Philadelphia (PA): Elsevier; 2014, p. 43-56.
- Silini AR, Di Pietro R, Lang-Olip I, Alviano F, Banerjee A, Basile M, et al. Perinatal Derivatives: Where Do We Stand? A Roadmap of the Human Placenta and Consensus for Tissue and Cell Nomenclature. *Front Bioeng Biotechnol.* 2020;8:610544. doi: 10.3389/fbioe.2020.610544.
- Chitra T, Sushanthi YS, Raghavan S. Umbilical coiling index as a marker of perinatal outcome: an analytical study. *Obstet Gynecol Int.* 2012;2012:213689. doi: 10.1155/2012/213689.
- Cromi A, Ghezzi F, Dürig P, Di Naro E, Raio L. Sonographic umbilical cord morphology and coiling patterns in twin-twin transfusion syndrome. *Prenat Diagn.* 2005;25(9):851-5. doi: 10.1002/pd.1273.
- Damascono EB, de Lima PP. Wharton's jelly absence: a possible cause of stillbirth. *Autops Case Rep.* 2013;3(4):43-7. doi: 10.4322/acr.2013.038.
- Cheng T, Yang B, Li D, Ma S, Tian Y, Qu R, et al. Wharton's Jelly Transplantation Improves Neurologic Function in a Rat Model of Traumatic Brain Injury. *Cell Mol Neurobiol.* 2015;35(5):641-9. doi: 10.1007/s10571-015-0159-9.
- Edmonds HW. The spiral twist of the normal umbilical cord in twins and in singletons. *Am J Obstet Gynecol.* 1954;67(1):102-20. doi: 10.1016/0002-9378(54)90201-x.
- Subashini G, Anitha C, Gopinath G, Ramyathangam K. A Longitudinal Analytical Study on Umbilical Cord Coiling Index as a Predictor of Pregnancy Outcome. *Cureus.* 2023;15(3):e35680. doi: 10.7759/cureus.35680.
- Laat MW, Franx A, Bots ML, Visser GH, Nikkels PG. Umbilical coiling index in normal and complicated pregnancies. *Obstet Gynecol.* 2006;107(5):1049-55. doi: 10.1097/01.AOG.0000209197.84185.15.
- Jo YS, Jang DK, Lee G. The sonographic umbilical cord coiling in late second trimester of gestation and perinatal outcomes. *Int J Med Sci.* 2011;8(7):594-8. doi: 10.7150/ijms.8.594.
- Kumar A, Bhat V, Kumar A. Umbilical cord coiling index at term gestation and its association with perinatal outcomes. *Ind J Public Health Res Dev.* 2022;(13):69-76.
- Suvarna S, Kim, Layton Christopher, Bancroft Johan. *Bancroft's Theory and Practice of Histological Techniques: 9th Ed.* Elsevier; 2019, p. 173-86.
- Frossi B, Mion F, Sibillano R, Daneli L, Pucillo CEM. Is it time for a new classification of mast cells? What do we know about mast cell heterogeneity? *Immunol Rev.* 2018;282(1):35-46. doi: 10.1111/immr.12636.
- Piliiponsky AM, Acharya M, Shubin NJ. Mast Cells in Viral, Bacterial, and Fungal Infection Immunity. *Int J Mol Sci.* 2019;20(12):2851. doi: 10.3390/ijms20122851.
- Komi DEA, Khomtchouk K, Santa Maria PL. A Review of the Contribution of Mast Cells in Wound Healing: Involved Molecular and Cellular Mechanisms. *Clin Rev Allergy Immunol.* 2020;58(3):298-312. doi: 10.1007/s12016-019-08729-w.
- Kornstädt L, Pierre S, Weigert A, Ebersberger S, Schäufele TJ, Kolbinger A, et al. Bacterial and Fungal Toll-Like Receptor Activation Elicits Type I IFN Responses in Mast Cells. *Front Immunol.* 2021;11:607048. doi: 10.3389/fimmu.2020.607048.
- Grootens J, Ungerstedt JS, Nilsson G, Dahlin JS. Deciphering the differentiation trajectory from hematopoietic stem cells to mast cells. *Blood Adv.* 2018;2(17):2273-81. doi: 10.1182/bloodadvances.2018019539.
- Stefańska K, Ozegowska K, Hutchings G, Popis M, Moncrieff L, Dompe C, Janowicz K, et al. Human Wharton's Jelly-Cellular Specificity, Stemness Potency, Animal Models, and Current Application in Human Clinical Trials. *J Clin Med.* 2020;9(4):1102. doi: 10.3390/jcm9041102.

Стаття надійшла до редакції 15.05.2024. – Дата першого рішення 22.05.2024. – Стаття подана до друку 27.06.2024