The Egyptian Journal of Hospital Medicine (July 2025) Vol. 100, Page 3724-3728

Vitamin B5 (Pantothenic Acid) as a New Insight and Treatment of Oligohydramnios

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ABSTRACT

Background: Oligohydramnios has low amniotic fluid volume, and causes neonatal comorbidity. Vitamin B5, is a water-soluble vitamin involved in metabolism. Aquaporin 1 (AQP1) is a water channel protein. Protein kinase B (AKT) is a signalling molecule involved in multiple cellular processes.

Objectives: To assess the clinical efficacy of vitamin B5 in the treatment of idiopathic oligohydramnios and its related adverse fetal/neonatal outcomes, and investigating the role of AQP1 and AKT1 in idiopathic oligohydramnios pathogenesis.

Patients and methods: Vitamin B5 was given to group 1 (n=80), while group 2 (n=63) received placebo as a control group. Patients of both groups have idiopathic oligohydramnios. The amniotic fluid index (AFI), mode of delivery, and perinatal outcome were documented. The gene expression levels of AQP1 and AKT1 were assayed in subgroups (G1a), and (G2a) of 8 idiopathic oligohydramnios patients each, where G1a got vitamin B5, and G2a got placebo. In addition to group 3 of 8 normal pregnant females.

Results: In group 1, AFI was increased in 76.2 %, steady in 22.6 %, and decreased in 1.2 % of patients; while in group 2, AFI was steady in 6.4 %, and decreased in 93.6 % of patients. Group 2 showed significant decline in normal vaginal delivery, and rise in lower segment caesarean section (LSCS) in comparison with group 1. The current study showed significant changes in gene expression levels of AQP1, and AKT1 among studied groups.

Conclusion: Vitamin B5 acted as effective treatment in idiopathic oligohydramnios. AQP1 and AKT1 may contribute in idiopathic oligohydramnios pathogenesis.

Keywords: Amniotic fluid index, Oligohydramnios, Maximum vertical pocket, Pantothenic acid.

INTRODUCTION

Amniotic fluid acts as a fetal physical cushion and, provides nutrients for fetal growth. Amniotic fluid volume (AFV) increases up to 400-1200 ml at 34-38 weeks of gestation **(1)**. Non-invasive evaluation methods of AFV include the four-quadrant amniotic fluid index (AFI), the diameter of the single deepest pocket (SDP), and the two-diameter pocket **(2)**.

Oligohydramnios is characterized by reduced AFV less than 5% for gestational age **(3)**. It is accompanied with poor fetal/neonatal outcomes [(4)].

It can be diagnosed with ultrasound, if AFI is less than 5 cm; or if the maximum deepest pocket is less than 2 cm. The best method of diagnosis of oligohydramnios is the diameter of the SDP. However, most publications use AFI [(3)]. Vitamin B5 (pantothenic acid) is a water-soluble vitamin, which is naturally available in some foods, and can be synthesized by intestinal microflora[(5)]. Its main function is to synthesize coenzyme-A, which is necessary for the transmission of acetyl and acyl groups in metabolic processes [(6)]. Alterations in the CoA-SH/acetyl-CoA ratio affect mitosis, autophagy, and cell death[(7)]. Free CoA-SH is involved in protein CoAlation, which acts as reversible post translational modification that protects surface-exposed cysteine residues from irreversible overoxidation. Thus, it is related to redox regulation [(8)]. Pantothenic acid also triggers immune cells to produce cytokines [(9)].

Aquaporins are membrane-bound water channel proteins that regulate the water flow across biological membranes[(10)]. Classical AQPs (AQP0, 1, 2, 4, 5, 6, and 8) are only water permeable. However, aquaglyceroporins (AQP3, 7, 9, and 10) allow the transport of water, urea, glycerol, ammonia, reactive oxygen species, and carbon dioxide [(11)]. The most abundant aquaporin in human amnion is AQP1[(12)].

Protein kinase B (AKT) is a serine/threonine kinase that regulates cell survival, and metabolism. The human AKT genes include AKT1, AKT2, and AKT3[(13)]. Phosphatidylinositol 3-kinase (PI3K)–AKT signalling regulates the vitamin B5 transporter, named sodium-dependent multivitamin transporter (SMVT). PI3K–AKT signalling affects CoA biosynthesis by regulating the rate limiting enzyme pantothenate kinase 2 (PANK2) [(14)].

The objective of the present study is to determine the clinical efficacy of vitamin B5 in the treatment of idiopathic oligohydramnios and its related adverse fetal/neonatal outcomes. In addition to investigating the role of AQP1 and AKT1 in oligohydramnios pathogenesis, as effective treatment of idiopathic oligohydramnios is hampered by the lack of understanding of molecular mechanisms that trigger this condition.

PATIENTS AND METHODS

Study design:

The current study was carried out in the antenatal care unit of the Gynaecology and Obstetrics Department, Faculty of Medicine, Tanta University, starting in May 2023. It included 143 pregnant women

Received: 16/04/2025
Accepted: 24/06/2025

with idiopathic oligohydramnios, and 8 normal pregnant women. Patients were allocated into two main groups. Group 1 (G1) comprised 80 women with idiopathic oligohydramnios who received vitamin B5 (pantothenic acid) (bepanthene) at a dose of 500 mg/2 ml ampoule, every 3 days. Bepanthene ampoule purchased from Bayer Company, Switzerland. Group 2 (G2) comprised 63 pregnant women with idiopathic oligohydramnios who received placebo (saline 2ml every 3 days).There were no conditions that could affect the objectivity of the study. Quantification of gene expression of AQP-1, and AKT-1, was conducted for subgroups (G1a) for patients of idiopathic oligohydramnios who received vitamin B5, and (G2a) for patients with idiopathic oligohydramnios who received placebo. Each group had 8 patients. In addition to having a third group (G3) of eight normal pregnant women for gene expression assay.

Complete patient history was taken including personal, and obstetric history, previous lethal congenital anomalies, and previous oligohydramnios. Oligohydramnios was diagnosed through history taking, clinical examination, and ultrasonography. All basic demographic data, and data concerning mode of delivery, perinatal outcome, AFI changes, degree of oligohydramnios were collected.

Inclusion criteria:

Age of patients between 18-35 years, idiopathic oligohydramnios, gestational age ≥24 weeks, patients wishing continuation of pregnancy.

Exclusion criteria:

Premature rupture of membranes, any lethal congenital anomaly, systemic diseases as preeclampsia or hypertension, diabetes mellitus and systemic lupus erythematosus.

Measurement of response to treatment:

(i) Amniotic fluid index (AFI): The four quadrants of the uterus were systematically examined. The ultrasound transducer was held perpendicular to patient's spine, not skin to ensure the measurement of all fluid pockets in same plane. The application of color Doppler over the pocket aimed to exclude the presence of any umbilical cord segments. The calipers should not cross over any fetal parts or any umbilical cord segment. In each quadrant, the deepest vertical pocket of fluid was identified and measured. In order to calculate the total AFI, the measurements of the four quadrants were added. Oligohydramnios was considered, if AFI was ≤5 [(15)].

(ii) Maximum vertical pocket (MVP): The single largest vertical fluid pocket was identified and measured. Under normal conditions, the single deepest pocket is two to eight cm (In oligohydramnios, it is <2 cm) [(15)].

Tissue sampling:

Placental tissues from patients enrolled in subgroups (G1a), (G2a), and (G3) were collected immediately after labour. They were cut into pieces and kept frozen at -80 for further quantification of gene expression.

Purification of RNA and gene expression assay by quantitative Real-Time Polymerase Chain Reaction (qRT-PCR):

TRIzol reagent was utilized for total RNA extraction from placenta (Invitrogen, Carlsbad, CA, USA, 15596026) according to the recommendations of manufacturer. NanoDrop spectrophotometer (NanoDrop Technologies, USA) was utilized for the assay of RNA purity and concentration. RNA was reverse-transcribed using Revert Aid H Minus Reverse Transcriptase (Thermo Scientific, #EP0451, Waltham, MA, USA). The newly synthesized cDNA was subsequently amplified by PCR using SYBR Green qPCR Master Mix (Thermo Scientific, USA, catalog number K0221), according to the instructions of manufacturer. Step One Plus real-time PCR system (from Applied Biosystem, USA) was used. Relative fold change levels were determined using the $2^{-\Delta\Delta CT}$ method [(16)], with glyceraldehyde 3 phosphate dehydrogenase (GAPDH) used as housekeeping genes. The primer sequences of the used genes [(17,18)] are listed in table 1.

Table 1: Primer sequences of used genes.

Gene	Primer sequence
AQP1	Forward: 5′-GGTGGGGAACAACCAGACG-3′ Reverse: 5′-TACATGAGGGCACGGAAGATG-3′
AKT1	Forward: 5′- TCTATGGCGCTGAGATTGTG -3′ Reverse: 5′- CTTAATGTGCCCGTCCTTGT -3′
GAPDH	Forward: 5′- ACGGATTTGGTCGTATTGGG -3′ Reverse: 5′- CGCTCCTGGAAGATGGTGAT-3′

Ethical approval:

Tanta Faculty of Medicine Ethical Committee approved the current study (approval code:36264PR206/05/23) before enrolment. Written informed consents were obtained from all patients. The Helsinki Declaration was followed throughout the study's conduct.

Statistical methods

Data analysis was carried out by Statistical Package for the Social Sciences (SPSS) version 26 (IBM Inc., Armonk, NY, USA). Categorical variables were presented as frequency and percentage (%) and were analysed utilizing the chi-square test. Quantitative numerical variables were expressed as mean ± standard deviation (±SD). The unpaired Student's t-test was used for comparing both groups (G1) and (G2). One way ANOVA test was used for comparing (G1a), (G2a), and

(G3) subgroups for gene expression analysis, followed by post hoc test **Tukey's HSD (Honestly Significant Difference) test** for pairwise comparison. Data were considered statistically significant, if the P value was < 0.05.

RESULTS

Demographic data and mode of delivery among the studied groups:

There was an insignificant difference between both groups concerning age, and body mass index (BMI). In group1, normal vaginal delivery represented 62.5 % followed by lower segment caesarean section (LSCS), which represented 33.7 %. Normal labour was significantly lower in group 2 compared to group 1. LSCS was significantly higher in group 2 compared to group 1. There was an insignificant difference between both groups as regards vaginal birth after caesarean section, as illustrated in table 2.

AFI changes among the studied groups:

AFI changes was significantly different between both groups. In group 1, AFI was increased in 61 case (76.2 %) patients, while in group 2, AFI was not increased at all, as illustrated in table 2.

Association of degree of oligohydramnios among the studied groups:

Degree of oligohydramnios was significantly different between both groups. In group 1 moderate oligohydramnios (2.1-5 cm) occurred in 49 (61.2 %) patients, while in group 2, moderate oligohydramnios (2.1-5 cm) occurred in 51 (81%) patients, as illustrated in table 2.

Table 2: Demographic and clinical data within studied groups

		Group 1 (n= 80)	Group 2 (n= 63)	P value
Age (years)		29.71 ± 4.63	28.93± 4.63	0.113
BMI (Kg/m2)		27.55 ± 2.78	27.2 ± 3.07	0.256
Mode of delivery	**Normal labour**	50 (62.5%)	3 (4.7%)	<0.001*
	LSCS	27 (33.7%)	60 (95.2%)	<0.001*
	VBAC	3 (2.4%)	0 (0%)	0.114
AFI changes	**Increased**	61 (76.2 %)	0 (0%)	<0.001*
	Steady	18 (22.6 %)	4 (6.4 %)	
	Decreased	1 (1.2 %)	59 (93.6 %)	
Degree of Oligohydramnios	**Moderate (2.1-5 cm)**	49 (61.2%)	51(81%)	0.011*
	Severe (<2 cm)	31 (38.8%)	12 (19%)	

BMI: Body mass index, LSCS: lower segment caesarean section, VBAC: vaginal birth after caesarean delivery, AFI: Amniotic fluid index, *: statistically significant.

Perinatal outcome in the studied groups:

The perinatal outcome was significantly different between both groups. Alive and healthy babies' percentage was significantly lower in group 2 compared to group 1. However, intrauterine deaths and neonatal intensive care unit (NICU) admissions were significantly higher in group 2 compared to group 1, as illustrated in table 3.

Table 3: Perinatal outcome within studied groups.

		Group 1 (n= 80)	Group 2 (n= 63)	P value
Perinatal outcome	**Alive and healthy**	76 (95%)	27 (42.9%)	<0.001*
	Intrauterine deaths	1 (1.2%)	11 (17.4%)	<0.001*
	NICU admissions	3 (3.8%)	25 (39.7%)	<0.001*

NICU: Neonatal intensive care unit, *: statistically significant.

Gene expression of AQP1 and AKT1:

Gene expression levels of AQP1 and AKT1 were assayed as fold changes in groups (G1a), (G2a), and (G3). The current study displayed significant upregulation of the gene expression level of AQP1 in placentas of oligohydramnios patients who received vitamin B5 in (G1a) group, compared to oligohydramnios patients who received placebo in (G2a) group. However, the gene expression levels of AQP1 were downregulated in (G2a) group, compared to (G3) group of normal pregnancy.

The present research displayed decline of gene expression levels of AKT1 in (G1a) group, compared to (G2a). However, there was increased gene expression level of AKT1 in oligohydramnios patients of (G2a) group compared to (G3) group of normal pregnancy.

Table 4: Gene expression of AQP1, and AKT1 among groups (G1a), (G2a), and (G3):

	Group 1a (n= 8)	Group 2a (n= 8)	Group 3 (n= 8)	P value
AQP1	0.98 ± 0.28	0.55 ^{a} ± 0.11	1^{b} ± 0	<0.001*
AKT 1	1.93 ± 0.37	3.38^{a} ± 0.58	1^{ab} ± 0	<0.001*

AQP1: aquaporin1, AKT 1: protein kinase B, *: statistically significant. a: significant with group (1a), b: significant with group (2a).

DISCUSSION

Vitamin B5 is a water-soluble vitamin necessary for CO-A synthesis [5,6]. The current study aims to assess the clinical efficacy of vitamin B5 in the treatment of idiopathic oligohydramnios and its related adverse fetal and neonatal outcomes. In addition to investigating the role of AQP1 and AKT1 in the pathogenesis of oligohydramnios.

Amniotic fluid safeguards fetal growth [18]. The present study found a significant effect of vitamin B5 (pantothenic acid) on AFI changes and perinatal outcomes in pregnant women with idiopathic oligohydramnios. AFI changes were significantly different between both groups. As in (G1) group, AFI was increased in 61 (76.2 %) patients, steady in 18 (22.6 %) patients, and decreased in 1 (1.2 %) patient. While in (G2) group, AFI was steady in 4 (6.4 %) patients, and decreased in 59 (93.6%) patients. Intrauterine deaths and NICU admissions were significantly higher in (G2) group compared to (G1) group (P<0.001). Normal labour was significantly higher in (G1) group compared to (G2) group (P<0.001) due to increasing AFI, possibly by the effect of vitamin B5. LSCS was significantly higher in (G2) group compared to (G1) group (P<0.001). The perinatal outcome was significantly different between both groups, as alive and healthy babies were significantly lower in (G2) group compared to (G1) group (P<0.001). This could be reinforced by the study of **Ghonem *et al.*** [19], **Elbaz *et al.*** [20], and **Saxena *et al.*** [21] who found that oligohydramnios displayed a higher risk of perinatal morbidity. According to **Yenigul *et al.*** [22], pregnancies with isolated oligohydramnios are not at high risk for cesarean delivery. However, the rate of cesarean section performed due to fetal distress increased.

To the knowledge of the authors, no studies were conducted before to evaluate the impact of vitamin B5 on AFI. Concerning the perinatal effects of vitamin B5, the decline of vitamin B5 level in amniotic fluid of mother mice with cleft palate children, was documented, when compared to its level in mother mice with healthy fetuses [23].

The current study displayed downregulation of the gene expression level of AQP1in placentas of oligohydramnios patients who received placebo (G2) compared to G3, which comprises normal pregnant women. This aligns with the study of **Luo *et al.*** [24] that documented the dramatic reduction of AQP1 gene expression in placentas and foetal membranes of patients with isolated oligohydramnios compared to normal pregnancies. **Di Paola *et al.*** [12] observed the dramatic decrease of transcellular water transport in human amnion, that results from blockage of AQP1, which suggests the contribution of AQP1 in passive intramembranous water transfer. In post term pregnancies, alteration in the expression of AQP1 on amnion, placenta and chorion are thought to be responsible for the reduction in amniotic fluid [4]. Vitamin B5 administration was accompanied by increased expression of AQP1 in the current study. This could be supported by the results of **Özden *et al.*** [25] who documented that dexpanthenol, a pantothenic acid analog, can restore levels of AQP2 in acute kidney injury.

The present research displayed increased gene expression level of AKT1 in group (2a) oligohydramnios patients who received placebo, compared to (G3) group of normal pregnancies. This could be supported by the research of **Cheung and Brace** [26] who declared the activation of PI3K/AKT signalling in amnion of oligohydramnios patients.

In the current study, the decline of AKT1 level following vitamin B5 administration, is in harmony with the results of **Ma *et al.*** [27] who documented that PI3K-Akt signalling showed remarkable activation, following pantothenic acid treatment at the concentration of 200 µM but at the concentration of 1000 µM, PI3K displayed marked suppression.

The current study possesses multiple strengths, including large sample size, meticulous follow up for all cases, measurement of AFI, and investigating the role of gene expression of AQP1, and AKT1 in the pathogenesis of oligohydramnios, which could provide the scientific basis for future pharmacologic interventions. The limitations include the shortage of studies discussing the effect of vitamin B5 on oligohydramnios for comparison, although it indicates

the novelty of the study aspect. It is recommended to study the impact of vitamin B5 on oligohydramnios through modulating immunity and redox status, which could provide further explanation of its role. It is also recommended to study the effect of vitamin B5 on various types of aquaporins, including AQP3, and AQP9, in oligohydramnios.

CONCLUSION

Overall, the current study findings showed that vitamin B5 can improve the pregnancy outcomes in women with idiopathic oligohydramnios. The gene expression of AQP1, and AKT1 was altered in oligohydramnios groups compared to normal pregnancy. Vitamin B5 administration induced significant changes in their gene expression levels, which indicates that, these genes may contribute in the pathogenesis of oligohydramnios.

No funding.

No conflict of interests.

REFERENCES

1. **Shamsnajafabadi H, Soheili Z (2022):** Amniotic fluid characteristics and its application in stem cell therapy: A review. Int J Reprod Biomed., 20(8):627-643.
2. **Miremberg H, Grinstein E, Herman H *et al.* (2020):** The association between isolated oligohydramnios at term and placental pathology in correlation with pregnancy outcomes. Placenta, 90:37-41.
3. **Huri M, Di Tommaso M, Seravalli V (2023):** Amniotic fluid disorders: From prenatal management to neonatal outcomes. Children (Basel), 10(3):561.
4. **Twesigomwe G, Migisha R, Agaba D *et al.* (2022):** Prevalence and associated factors of oligohydramnios in pregnancies beyond 36 weeks of gestation at a tertiary hospital in southwestern Uganda. BMC Pregnancy Childbirth, 22(1):610.
5. **Munteanu C, Berindean I, Mihai M, *et al.* (2023):** K, B5, B6, and B9 vitamins and their specific immunological effects evaluated by flow cytometry. Front Med (Lausanne), 9:1089476.
6. **Yu Y, van der Zwaag M, Wedman J *et al.* (2022):** Coenzyme A precursors flow from mother to zygote and from microbiome to host. Molecular Cell, 82(14): 2650-2665.e12.
7. **Naquet P, Kerr E, Vickers S *et al.* (2020):** Regulation of coenzyme A levels by degradation: the 'Ins and Outs'. Prog Lipid Res,78:101028.
8. **Brett C, Gout I (2025):** The two faces of coenzyme A in cellular biology. Free Radical Biology and Medicine, 233: 162-173.
9. **Gheita A, Gheita T, Kenawy S (2020):** The potential role of B5: A stitch in time and switch in cytokine. Phytother Res., 34(2): 306-314.
10. **Zannetti A, Benga G, Brunetti A (2020):** Role of aquaporins in the physiological functions of mesenchymal stem cells. Cells, 9(12):2678.
11. **Pimpão C, Wragg, D, da Silva I *et al.* (2022):** Aquaglyceroporin modulators as emergent pharmacological molecules for human diseases. Frontiers in Molecular Biosciences, 9:845237.
12. **Di Paola M, Sierra M, Fernández N *et al.* (2022):** Contribution of aquaporins in the transamniotic water flux. Biochem Biophys Res Commun., 590: 63-67.
13. **Hassan D, Menges C, Testa J *et al.* (2024):** AKT kinases as therapeutic targets. J Exp Clin Cancer Res., 43: 313.
14. **Barritt S, DuBois-Coyne S, Dibble C (2024):** Coenzyme A biosynthesis: mechanisms of regulation, function and disease. Nature Metabolism, 6(6): 1008-1023.
15. **Elsadek A, Atef A, Salama D *et al.* (2022):** Sonography assessment of amniotic fluid volume as a predictor of fetal outcome in low-risk pregnancy. The Egyptian Journal of Hospital Medicine, 88(1): 3022-3028
16. **Livak K, Schmittgen T (2001):** Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. Methods, 25(4): 402-8.
17. **Vassiliou A, Maniatis N, Orfanos S *et al.* (2013):** Induced expression and functional effects of aquaporin-1 in human leukocytes in sepsis. Critical Care, 17(5): R199.
18. **Riquelme I, Tapia O, Espinoza J (2016):** The gene expression status of the PI3K/AKT/mTOR pathway in gastric cancer tissues and cell lines. Pathol Oncol Res., 22(4):797-805.
19. **Ghonem M, El-shourbagy S, Al- Namoury M *et al.* (2025):** Correlation between amniotic fluid volume in women with forewater preterm premature rupture of membranes and perinatal outcomes. Evidence Based Women's Health Journal, 15(15): 1-7.
20. **Elbaz E, Eltotongy M, Ghanem A *et al.* (2025):** The Effect of β-sympathomimetics on amniotic fluid volume in women with idiopathic oligohydramnios. Evidence Based Women's Health Journal, 15(15):1-6.
21. **Saxena R, Patel B, Verma A (2020):** Oligohydramnios and its perinatal outcome. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 9(12): 4965- 4969.
22. **Yenigul N, Asicioglu O (2019):** The Effects of isolated oligohydramnios in term pregnancies on labor, delivery Mode, and neonatal outcomes. Eurasian Journal of Medical Investigation, 3: 59-64.
23. **Scheller K, Quitzke V, Kappler M (2018):** New molecular aspects in the mechanism of oromaxillofacial cleft prevention by B-vitamins. J Craniomaxillofac Surg., 46(12):2058-2062.
24. **Luo H, Liu Y, Song Y *et al.* (2020):** Aquaporin 1 affects pregnancy outcome and regulates aquaporin 8 and 9 expressions in the placenta. Cell and Tissue Research, 381(3): 543-554.
25. **Özden E, Aşcı H, Büyükbayram H (2023):** Dexpanthenol protects against lipopolysaccharide-induced acute kidney injury by restoring aquaporin-2 levels via regulation of the silent information regulator 1 signaling pathway. Korean J Anesthesiol., 76(5):501-509.
26. **Cheung C, Brace R (2020):** Altered proteomics profile in the amnion of patients with oligohydramnios. Physiological Reports, 8(4): e14381.
27. **Ma Q, Liang M, Tang X (2019):** Vitamin B5 inhibit RANKL induced osteoclastogenesis and ovariectomy induced osteoporosis by scavenging ROS generation. Am J Transl Res., 11(8):5008-5018.