International Journal of Research in Medical Sciences
Abbas MW et al. Int J Res Med Sci. 2016 Jan;4(1):5-11
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20160002

Review Article

Diabetes insipidus: the basic and clinical review

Muhammad Waseem Abbas[1]*, Muhammad Arslan Iqbal[2], Muhammad Nouman Iqbal[2], Rukhsar Javaid[1], Muhammad Aizaz Ashraf[1]

[1]Nishtar Medical College, Multan, Pakistan
[2]Multan Medical and Dental College, Multan, Pakistan

Received: 12 November 2015
Revised: 20 November 2015
Accepted: 17 December 2015

***Correspondence:**
Dr. Muhammad Waseem Abbas,
E-mail: wiz46221@outlook.com

ABSTRACT

Diabetes insipidus (DI) is a complex disease. DI is inability of the body to conserve water. Polydipsia and polyuria are the major manifestations of DI. DI has various variants including central diabetes insipidus (due to defect in ADH secretion), nephrogenic diabetes insipidus (due to defect in ADH receptors or urea receptors), gestational diabetes insipidus (due to catabolism of ADH by placental vasopressinase) and primary polydipsia (due to massive fluid intake). The cause of various variants of DI is either acquired or congenital. High plasma osmolality due to hypotonic urine excretion can be fatal because it can cause psychosis, lethargy, seizures, coma or even death. Polyuria and polydipsia help in the diagnosis of DI. Differential diagnosis of various variants of DI can be carried out on the basis of water deprivation test, MRI and other radiological techniques. The proper management of DI is the replenishment of water loss and correction of clinical presentations produced as a result of DI, major is hypernatremia. The best management for primary polydipsia is fluid restriction while fluid intake is used for adipsic diabetes insipidus. ADH replacement therapy is widely used to treat DI. DDAVP or desmopressin is mostly preferred ADH analogue because it has less side effects and resistant to placental vasoprssinase.

Keywords: Diabetes, Desmopressin, Vasopressinase, Hypernatremia, MRI

INTRODUCTION

Diabetes Insipidus (DI) is a very complex and rare disease. The word "Diabetes Insipidus" is a combination of two words "Diabetes" and "Insipidus". Diabetes is a word of Greek origin which means "siphon" and Insipidus is a word of Latin origin which means "without taste".[1] DI is actually inability of body to conserve water due to pathophysiology of production of antidiuretic hormone (ADH) and its action.[2] ADH is produced by the neurons of supraoptic and paraventricular nuclei located in the hypothalamus. After the production ADH streamlines down along the hypothalmo-hypophyseal tract and is stored in posterior pituitary, which on proper stimulus from osmoreceptors, is released from its storage location.[3] The production, storage and release of ADH are shown in Figure 1(a).[4] Polydipsia, polyuria, hypernatremia, dehydration and severe thirst are most common manifestations of DI.[1,5-8] The incidence of DI in general population is about 3:100, 000.[9]

Types of diabetes insipidus (DI)

The Diabetes insipidus include following types[10]

1 Neurogenic diabetes insipidus
2 Nephrogenic diabetes insipidus
3 Gestational diabetes insipidus
4 Adipsic diabetes insipidus
5 Primary polydipsia
6 Dipsogenic diabetes insipidus
7 Psychogenic diabetes insipidus

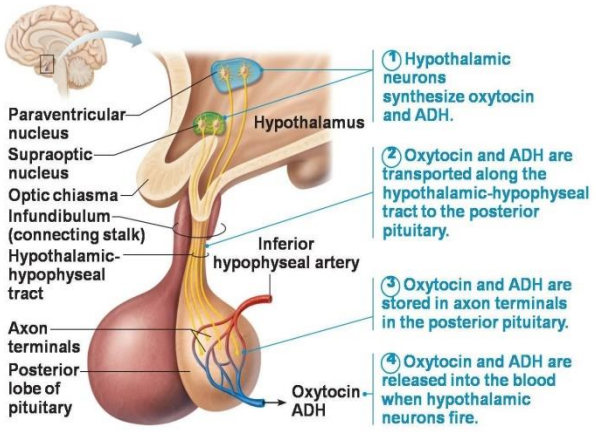

Figure 1(a): 1. Production site, 2. hypothalmo-hypophyseal tract, 3. storage location and 4. release.

Neurogenic diabetes insipidus

Neurogenic diabetes insipidus is most commonly known as Central Diabetes Insipidus (CDI). In CDI person is unable to conserve water due to decreased synthesis of anti-diuretic hormone (ADH) or Arginine Vasopressin (AVP).[2] CDI can be lethal due to its complications occurred due to hypernatremia and high plasma osmolality.[11]

Etiology

The major cause of CDI is traumatic brain injury (TBI) leading to the damage of hypothalamo-neurohypophyseal region.[12,13] Surgery and tumors of supraoptic and paraventricular nuclear region can also be the cause of CDI.[14,15] CDI can also be due to the congenitally inherited mutations of prepro-vasopressin-neurophysin II gene involving the substitution of glycine for valine.[16] The other causes are autoimmunity, histocytosis, granulomatosis, sarcodosis and alcohol.[11]

Clinical presentations

Polyuria and polydipsia are the main clinical manifestations involved in CDI.[17] High production of urine leads to high plasma osmolality and life threatening hypernatremia and severe dehydration.[18] Compulsive thirst occurs in CDI.[2] There is assumption of occurrence of osteopenia due to diminished effect of prostaglandins and osteoblasts referring to the low ADH level.[19]

Nephrogenic diabetes insipidus

Nephrogenic diabetes Insipidus (NDI) is due to the insensitivity of kidneys in response to ADH.[9] Most of the adults have acquired form of NDI but the cause of NDI can also be congenital.[20]

Etiology

The congenital causes of NDI are the mutations of V2 receptor gene (X-linked), aquaporin-2 (AQP2) gene (autosomal-recessive) and urea transporter-B (UT-B) gene.[21-23] The X-linked inheritance is most commonly observable condition in males and these patients do not respond to DDAVP or desmopressin.[24] The acquired form of NDI is mainly due to lithium which is frequently used to treat bipolar disorders.[25,26] The other drugs characterized as the causing agents of NDI are Amphotericin B, Colchicines, Gentamicin, Methoxyflurane and Demaclocycline.[27,28] Acquired causes also include chronic renal failure, pyelonephritis, polycystic kidney disease, renal transplantation, obstructive uropathy, chronic renal medullary disease, chronic hypokalemia and chronic hypercalcemia.[29] Low protein diets also downregulate the AQP2 protein.[30-36]

Clinical Presentations

Due to the ADH insensitivity polyuria increases. The clinical presentation also includes nocturia.[11] Osmotic diuresis, leading to hypernatremia, hyperchloremia, constipation and prerenal azotemia, can cause mental retardation, seizures and death.[11,36]

Gestational diabetes insipidus

Gestational diabetes insipidus (GDI) is less frequently occurring type and only in pregnant women. The incidence of GDI is estimated to be the 5:100,000 of pregnancies.[37] Vasopressinase (enzyme) produced by placenta metabolizes the hormones of posterior pituitary both ADH and oxytocin.[38]

Etiology

Placenta produces a Vasopressinase. Vasopressinase is a cysteine aminopeptidase and it degrades the ADH and oxytocin. When this cysteine peptidase is produced in large amount, it catabolizes almost 99% quantity of produced oxytocin and ADH leading to GDI.[38]

Clinical presentations

Polydipsia, polyuria and severe thirst are common presentations of GDI. The association of GDI with preeclampsia and HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count) is most commonly observed.[39]

Adipsic diabetes insipidus

Adipsia is a disease in which there is an absence of thirst although body has dehydration and high plasma osmolality. Any lesion of thirst center in hypothalamus leads to the loss of thirst causing adipsia. Adipsia is often associated with CDI because the lesion of hypothalamus also affects the supraoptic and pavaventricular region (the

releasing sites of ADH). Hence, adipsia and CDI are collectively known as Adipsic diabetes insipidus (ADI).[40,41] It is very rare disease. In the world only 200 cases have been reported till now.[42]

Etiology

The main cause of ADI is the lesion of thirst center located in hypothalamus. Craniopharyngiomas affecting both thirst center and supraoptic and paraventricular region are important in causing the ADI.[43]

Clinical presentations

Patients suffering from ADI present with lack of thirst sensation with high plasma osmolality and hypernatremia. High sodium level can cause various complications including lethargy, mental disturbances, disturbed acid-base balance and even death.[43]

Primary polydipsia

Primary polydipsia (PP) is characterized by large amount of fluid intake. Large fluid intake leads to the low plasma osmolality and the production of ADH stops in response to low plasma osmolality. As a result of which the concentrating ability of kidneys fall down and person excretes large amount of dilute urine having low osmolality.[44,45]

Depending upon the cause of PP, it has two sub-variants:

- *Dipsogenic diabetes insipidus*

  Dipsogenic diabetes Insipidus (DDI) is a sub-variety of PP and it is caused by the defect in person's thirst center located in the hypothalamus. As a result of this defect, the thirst mechanism becomes overactive and person ingests large amount of fluid and discharges hypotonic urine.[44]

- *Psychogenic diabetes insipidus*

  Psychogenic diabetes Insipidus (PDI) is also a sub-variety of PP. It is mainly caused by psychiatric disorders like schizophrenia. Such psychiatric disorders lead a person to increase fluid intake and person then excretes highly dilute urine.[46,47]

Etiology

PP is mainly the large fluid intake. ADI is mainly caused due to the disturbance of thirst center[44] while the psychiatric disorders and psychiatric medications are important in PDI.[46,48,49] The side effects of psychiatric medications play an important role in PDI because these medications cause the dryness of mouth leading to high fluid intake. PP can also be due to some behavioral causes.[48,49]

Clinical presentations

Hypotonic polyuria is common manifestation of PP.[44] The other clinical presentations include polydipsia, intermittent hyponatremia and psychosis, the combination of these three is known as PIP syndrome.[45] Hyponatremia can be fatal and cause death.[44]

Differential diagnosis

According to the definition of DI, polyuria and hypotonic urine should be present. For the confirmation of polyuria, the urine output should be greater than 40ml/kg/24hrs.[17,50,51] For the confirmation of DI urine osmolality should be <300 mOsm/kg. Polyuria can be confirmed by the history of patient.[11,18] For differential diagnosis of various variants of DI, Water Deprivation Test is performed.[12,13] In order to perform this test person should be sufficiently dehydrated to stimulate ADH production and measure the volume and osmolality with each discharge until the weight decreases by 3% or plasma sodium level reaches 145mmol/L. Now, treat with desmopressin or DDAVP. If the concentration of urine rises by 50% or more then person is suffering from CDI if it increases by <10% then the diagnosis is NDI. If the osmolality of urine increases more than 750 mOsm then the patient is suffering from either CDI or PP. PP can be distinguished from CDI by the ability of a person to concentrate urine in response to dehydration while this concentrating ability is absent in CDI patients.[11,52] CDI can also be diagnosed with the help of MRI showing bright spot in sella turcica.[11,53,54] MRI and other radiological techniques help in the conformation of ADI.[43]

Management of diabetes insipidus

The proper management of DI involves the replenishment of water loss and correction of manifestations like hypernatremia produced as a result of DI. Thirst mechanism plays an important role in management of DI because water intake in response to thirst immediately corrects water loss but thirst mechanism is not much effective in unconscious patients and infants.[55] Hypernatremia should not be corrected too quickly because it can cause cerebral edema, seizures and death.[55] The rate at which hypernatremia is corrected should not be greater than 0.5mEq.[56] The best management for psychogenic and dipsogenic DI is fluid restriction [57] while adequate fluid intake is best proper management for adipsic diabetes insipidus.[58]

Therapeutic approaches

Neurogenic diabetes insipidus

ADH replacement is best therapeutic approach for CDI. Pitressin is purified form of ADH given intramuscularly for treatment of CDI. But now-a-days it is not frequently used due to its side effects including angina, hypertension

and abdominal cramping.[59,60] The most preferred replacement therapy is DDAVP (1-desamino-8-arginine vasopressin). It is also known as Desmopressin. It is preffered over pitressin and is resistant to placental vasopressinase.[11,38,61,62] Chlorpropamide also decreases the Polyuria by upto 75% and is used to treat the patients with mild CDI.[63,64] The other drugs which are used for treatment of mild form of CDI are Carbamazepine and Clofibrate.[59,60] Prostaglandin synthase inhibitors and thiazides are also used for treatment of CDI.[65]

Nephrogenic diabetes insipidus

Patients of NDI do not respond to ADH and desmopressin. The best therapeutic approach is to remove the causing agent like lithium etc, if causative agent of NDI is of acquired form.[11] Thiazides and amiloride are used for the treatment of lithium induced NDI.[66-69] Prostaglandin synthase inhibitors are used because they increase the AQP-2 channels at apical membrane by increasing intracellular cAMP level.[70,71] The main side effect of these drugs is that they cause kidney damage and gastric problems.[11,72,73] Recent studies have shown that long term treatment with thiazides can cause renal carcinoma.[73] Another treatment of NDI is the release of trapped V_2 receptors from endoplasmic reticulum. This can be done with the help of chemicals known as nonpeptide chaperones.[74,75] Recent studies have shown that gene therapy can be the better option for treatment of NDI but it is highly speculative.[24] Recent investigations have revealed that statins also increase the expression of AQP2 in apical membrane.[24]

Gestational Diabetes Insipidus

The best possible treatment of GDI is replacement of ADH by DDAVP.[37] DDAVP or desmopressin is resistant to placental vasopressinase.[76] DDAVP is frequently preferable because of its minute effect on maternal vascular tone but the recent studies have shown that the quantity of amniotic fluid may change.[77,78] Another treatment of GDI is by hydrochlorothiazide but it is usually not preferred because of its side effects including neonatal hypoglycemia and neonatal DI.[79]

Adipsic diabetes insipidus

DDAVP therapy is used to decrease the urine output in the patients of ADI. Moreover behavioral therapy is also required because the thirst mechanism fails to perform its function in patients of ADI.[80]

Primary polydipsia

Clozapine is an effective drug because it reduces the water intake but it is generally not preferred because of its side effects. Therefore fluid restriction is best management.[57]

CONCLUSION

Diabetes insipidus (DI) is not very common disease. Polyuria and polydipsia are common manifestations of DI due to inability of a person to conserve water. The cause of DI is either congenital or acquired. Water deprivation test and MRI are used for differential diagnosis. Water replenishment is best proper management of DI. Desmopressin or DDAVP is widely used ADH analogue in ADH replacement therapy to treat DI.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Muhammad Iqbal.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Chan JCM, Kemp S, Roth KS, Wilson TA. Pediatric diabetes Insipidus. Medescape. 2013.
2. Cagno JM. Diabetes insipidus. Crit Care Nurse. 1989;9:86-93.
3. Treschan TA Peters J. The vasopressin system: physiology and clinical strategies. Anesthesiology. 2006;105:599-612.
4. Gargan. Pituitary Gland and Hypothalamus. Biology 2402. Studyblue. Available at: https://www.studyblue.com/notes/note/n/04-pituitary-gland-andhyphothalamus/deck/1041967. Accessed 5th Nov 2015.
5. Saborio P, Tipton GA, Chan JCM. Diabetes Insipidus. Pediatric in Review. 2000;21:122-129.
6. Ghiradello S, Garre ML, Rossi A, Maghnie M. The diagnosis of children with central diabetes insipidus. J Pediatr Endocrinol Metab. 2007;20:359-75.
7. Di Largi N, Napoli F, Allergi A, Oliveri I, Bertteli C, Gallizia A et al. Diabetes Insipidus, diagnosis and management. Horm Res Pediatr. 2012;77:69-84.
8. Al Jurayyan NAM. The posterior pituitary gland In El Zouki A, Harfi H, Nazer H, eds; Textbook of Clinical Pediatrics. Lippincott William and Wilkins, Philadelphia, USA. 2001;1282-1284.
9. Arthus MF, Lonergan M, Crumley MJ, Naumova AK, Morin D. Report of 33 novel AVPR2 mutations and analysis of 117 families with X-linked nephrogenic diabetes insipidus. J Am Soc Nephrol. 2000;11:1044-54.
10. Yi-Chun Chou, Tzu-Yuan Wang, Li-Wei Chou. Diabetes Insipidus and Traumatic Brain Injury, Diabetes Insipidus. 2011; Available at: http://www.intechopen.com/books/diabetes-insipidus/diabetes-insipidus-and-traumaticbrain-injury. Accessed 6th Nov 2015.
11. Saborio P, Tipton GA, Chan JC. Diabetes Insipidus. Pediatr Rev. 2000;21:122-9.

12. Singer I, Oster JR, Fishman LM. The management of diabetes insipidus in adults. Arch Intern Med. 1997;157:1293-1301.
13. Adam P. Evaluation and management of diabetes insipidus. Am Fam Physician. 1997;55:2146-53.
14. Olson BR, Gumowski J, Rubino D, Oldfield EH. Pathophysiology of hyponatremia after transsphenoidal pituitary surgery. J Neurosurg. 1997;87:499-507.
15. Kristof RA, Rother M, Neuloh G, Klingmuller D. Incidence, clinical manifestations, and course of water and electrolyte metabolism disturbances following transsphenoidal pituitary adenoma surgery: a prospective observational study Clinical article. J Neurosurg. 2009;111:555-62.
16. Fujiwara TM, Morgan K, Bichet DG. Molecular biology of diabetes insipidus. Annu Rev Med. 1995;46:331-43.
17. Kerrebroeck VP, Abrams P, Chaikin D, Donovan J, Fonda D. The Standardisation of Terminology in Nocturia: report from the Standardisation Sub-Committee of the International Continence Society. Neurourol Urodyn. 2002;21:179-183.
18. Salata RA, Verbalis JG, Robinson AG. Cold water stimulation of oropharyngeal receptors in man inhibits release of vasopressin. J Clin Endocrinol Metab. 1987;65:561-567.
19. Pivonello R, Colao A, Di Somma C, Facciolli G, Klain M. Impairment of bone status in patients with central diabetes insipidus. J Clin Endocrinol Metab. 1998;83:2275-80.
20. Sands JM, Gargus JJ, Fro¨hlich O, Gunn RB, Kokko JP. Urinary concentrating ability in patients with Jk(a-b-) blood type who lack carrier-mediated urea transport. J Am Soc Nephrol. 1992;2:1689-96.
21. Forssman H. On the mode of hereditary transmission in diabetes insipidus. Nordisk Medicine. 1942;16:3211-3.
22. Waring AG, Kajdi L, Tappan V. Congenital defect of water metabolism. Am J Dis Child. 1945;69:323-5.
23. Williams RM, Henry C. Nephrogenic diabetes insipidus transmitted by females and appearing during infancy in males. Ann Intern Med. 1947;27:84-95.
24. Leonilde B, Giuseppe P, David Q-H W. A novel therapeutic effect of statins on nephrogenic diabetes insipidus. J. Cell. Mol. Med. 2015;19(2):265-82.
25. Timmer RT, Sands JM. Lithium intoxication. J Am Soc Nephrol. 1999;10:666-74.
26. Okusa MD, Crystal LJ. Clinical manifestations and management of acute lithium intoxication. Am J Med. 1994;97:383-9.
27. Kovacs L, Lichardus B. Vasopressin, Disturbed Secretion and Its Effects. Prague: Kluwer Academic Publishers. 1989.
28. Zhang Z, Kindrat AN, Sharif-Naeini R, Bourque CW. Actin filaments mediate mechanical gating during osmosensory transduction in rat supraoptic nucleus neurons. J Neurosci. 2007;27:4008-13.
29. Amgad NM, Samy IM. Diabetes insipidus: Diagnosis and treatment of a complex disease. Cleavland clinic journal of medicine. 2006;73(1):65-71.
30. Frøkiaer J, Marples D, Knepper MA, Nielsen S. Bilateral ureteral obstruction downregulates expression of vasopressin-sensitive AQP-2 water channel in rat kidney. Am J Physiol. 1996;270:657-68.
31. Sands JM, Flores FX, Kato A, Baum MA, Brown EM, Ward DT. Vasopressinelicited water and urea permeabilities are altered in IMCD in hyper-calcemic rats. Am J Physiol. 1998;274:978-85.
32. Marples D, Frøkiaer J, Dørup J, Knepper MA, Nielsen S. Hypokalemia induced down regulation of aquaporin-2 water channel expression in rat kidney medulla and cortex. J Clin Invest. 1996;97:1960-8.
33. Frøkiaer J, Christensen BM, Marples D, Djurhuus JC, Jensen UB, Knepper MA. Down regulation of aquaporin-2 parallels changes in renal water excretion in unilateral ureteral obstruction. Am J Physiol. 1997;273:213-23.
34. Earm JH, Christensen BM, Frøkiaer J, Marples D, Han JS, Knepper MA. Decreased aquaporin-2 expression and apical plasma membrane delivery in kidney collecting ducts of polyuric hypercalcemic rats. J Am Soc Nephrol. 1998;9:2181-93.
35. Amlal H, Krane CM, Chen Q, Soleimani M. Early polyuria and urinary concentrating defect in potassium deprivation. Am J Physiol Renal Physiol. 2000;279:655-63.
36. Sands JM, Naruse M, Jacobs JD, Wilcox JN, Klein JD. Changes in aquaporin-2 protein contribute to the urine concentrating defect in rats fed a low protein diet. J Clin Invest. 1996;97:2807-14.
37. El-Hennawy AS, Bassi T, Koradia N, BocirneaA. Transient gestational diabetes insipidus: report of two cases and review of pathophysiology and treatment. J Matern Fetal Neonatal Med. 2003;14:349-52.
38. Aleksandrov N, Audibert F, Bedard MJ, Mahone M, Goffinet F, et al. Gestational diabetes insipidus: a review of an underdiagnosed condition. J Obstet Gynaecol Can. 2010;32:225-231.
39. Peters M, Jeck N, Reinalter S, Leonhardt A, Tönshoff B, et al. Clinical presentation of genetically defined patients with hypokalemic salt-losing tubulopathies. Am J Med. 2002;112:183-190.
40. Verbalis JG, Berl T. Disorders of water balance. Brenner BM. The Kidney. 8. WB Saunders; 2007. 8.
41. Sinha A, Ball S, Jenkins A, Hale J, Cheetham T. Objective assessment of thirst recovery in patients with adipsic diabetes insipidus. Pituitary. 2011;14(4):307-11.
42. Mavrakis AN, Tritos NA. Diabetes insipidus with deficient thirst: report of a patient and review of the literature. Am J Kidney Dis. 2008;51(5):851-9.
43. Natascia DI, Flavia N, Anna Elsa MA. Diabetes Insipidus – Diagnosis and Management. Horm Res Paediatr. 2012;77:69-84.

44. Robertson GL. Differential diagnosis of polyuria. Annu Rev Med. 1998;39:425-42.
45. Goldman MB, Robertson GL, Luchins DJ, Hedeker D. The infuence of polydipsia on water excretion in hyponatremic, polydipsic, schizophrenic patients. J Clin Endocrinol Metab. 1996;81:1465-70.
46. Goldman MB, Luchins DJ, Robertson GL. Mechanisms of altered water metabolism in psychotic patients with polydipsia and hyponatremia. N Engl J Med. 1998;318:397-403.
47. Vieweg WV, Carey RM, Godleski LS, Tisdelle DA, Pruzinsky T. The syndrome of psychosis, intermittent hyponatremia, and polydipsia: Evidence for diurnal volume expansion. Psychol Med. 1990;8:135-144.
48. Valtin H. Drink at least eight glasses of water a day. Really? Is there scientific evidence for "8×8"? Am J Physiol Regul Integr Comp Physiol. 2002;283:993-1004.
49. Borghi L, Meschi T, Amato F, Briganti A, Novarini A. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. J Urol. 1996;155:839-43.
50. Weiss JP, Blaivas JG. Nocturia. J Urol. 2000;163:5-12.
51. Robertson GL. Diabetes insipidus. Endocrinol Metab Clin North Am. 1995;24:549-72.
52. Zerbe RL, Robertson GL. A comparison of plasma vasopressin measurements with a standard indirect test in the differential diagnosis of polyuria. N Engl J Med. 1981;305:1539-46.
53. Arslan A, Karaarslan E, Dincer A. High intensity signal of the posterior pituitary. A study with horizontal direction of frequency-encoding and fat suppression MR techniques. Acta Radiol. 1999;40:142-5.
54. Kurokawa H, Fujisawa I, Nakano Y, Kimura H, Akagi K. Posterior lobe of the pituitary gland: Correlation between signal intensity on T1-weighted MR images and vasopressin concentration. Radiology. 1998;207:79-83.
55. Arthus MF, Lonergan M, Crumley MJ, Naumova AK, Morin D. Report of 33 novel AVPR2 mutations and analysis of 117 families with X-linked nephrogenic diabetes insipidus. J Am Soc Nephrol. 2000;11:1044-54.
56. Blum D, Brasseur D, Kahn A, Brachet E. Safe oral rehydration of hypertonic dehydration. J Pediatr Gastroenterol Nutr. 1986;5:232-5.
57. Goldman MB. The assessment and treatment of water imbalance in patients with psychosis. Clin Schizophr Relat Psychoses. 2010;4:115-23.
58. Mentes JC. Hydration management. Iowa City (IA): University of Iowa Gerontological Nursing Interventions Research Center, Research Dissemination Core. 2004.
59. Gregerman RI. Selected endocrine problems. In: Barker LR, Burton JR, Zieve PD, editors. Principles of Ambulatory Medicine, 3rd edition. Baltimore, MD: Williams and Wilkins Publishers. 1991:997-998.
60. Seckl JR, Dunger DB. Diabetes insipidus. Current treatment recommendations. Drugs. 1992;44:216-24.
61. Fjellestad-Paulsen A, Hoglund P, Lundin S, Paulsen O. Pharmacokinetics of 1-deamino8-D-arginine vasopressin after various routes of administration in healthy volunteers. Clin Endocrinol (Oxf). 1993;38:177-182.
62. Brewster UC, Hayslett JP. Diabetes insipidus in the third trimester of pregnancy. Obstet Gynecol. 2005;105:1173-6.
63. Pokracki FJ, Robinson AG, Seif SM. Chlorpropamide effect: measurement of neurophysin and vasopressin in humans and rats. Metabolism. 1981;30:72-8.
64. Durr JA, Hensen J, Ehnis T, Blankenship MS. Chlorpropamide upregulates antidiuretic hormone receptors and unmasks constitutive receptor signaling. Am J Physiol Renal Physiol. 2000;278:799-808.
65. Rivkees SA, Dunbar N, Wilson TA. The management of central diabetes insipidus in infancy: desmopressin, low renal solute load formula, thiazide diuretics. J Pediatr Endocrinol Metab. 1999;20:459-69.
66. Loffing J. Paradoxical antidiuretic effect of thiazides in diabetes insipi¬dus: another piece in the puzzle. J Am Soc Nephrol. 2004;15:2948-50.
67. Kim GH, Lee JW, Oh YK, Chang HR, Joo KW. Antidiuretic effect of hydrochlorothiazide in lithium-induced nephrogenic diabetes insipidus is associated with upregulation of aquaporin-2, Na-Cl co-transporter, and epithelial sodium channel. J Am Soc Nephrol. 2004;15:2836-2843.
68. Karet FE. Disorders of water and acid-base homeostasis. Nephron Physiol. 2011;118:28-34.
69. Oliveira JL, Silva Júnior GB, Abreu KL, Rocha Nde A, Franco LF. Lithium Nephrotoxicity. Rev Assoc Med Bras. 2010;56:600-6.
70. Delaney V, Pertuz DY, Nixon D, Bourke E. Indomethacin in streptozocin-induced nephrogenic diabetes insipidus. Am J Kidney Dis. 1987;9:7983.
71. Kim GH, Choi NW, Jung JY, Song JH, Lee CH. Treating lithium induced nephrogenic diabetes insipidus with a COX-2 inhibitor improves polyuria via upregulation of AQP2 and NKCC2. Am J Physiol Renal Physiol. 2008;294:702-709.
72. Huerta C, Castellsague J, Varas-Lorenzo C, García Rodríguez LA. Nonsteroidal antiinflammatory drugs and risk of ARF in the general population. Am J Kidney Dis. 2005;45:531-539.
73. Zaki M, Schöneberg T, Al Ajrawi T, Al Said AN, Sangkuhl K. Nephrogenic diabetes insipidus, thiazide treatment and renal cell carcinoma. Nephrol Dial Transplant. 2006;21:1082-1086.
74. Los EL, Deen PM, Robben JH. Potential of nonpeptide (ant) agonists to rescue vasopressin V2 receptor mutants for the treatment of X-linked

nephrogenic diabetes insipidus. J Neuroendocrinol. 2010;22:393-9.
75. Morello JP, Bichet DG. Nephrogenic diabetes insipidus. Annu Rev Physiol. 2001;63:607-30.
76. Durr JA, Hoggard JG, Hunt JM, Schrier RW. Diabetes insipidus in pregnancy associated with abnormally high circulating vasopressinase activity. N Engl J Med. 1987;316:1070-4.
77. Hanson RS, Powrie RO, Larson L. Diabetes insipidus in pregnancy: a treatable cause of oligohydramnios. Obstet Gynecol. 1997;89:816-7.
78. Ross MG, Cedars L, Nijland MJ, Ogundipe A. Treatment of oligohydramnios with maternal 1-deamino-[8-D-arginine] vasopressin-induced plasma hypoosmolality. Am J Obstet Gynecol. 1996;174:1608-13.
79. Sainz Bueno JA, Villarejo Ortiz P, Hidalgo Amat J, Caballero Fernandez V, Caballero Manzano M, Garrido Teruel R. Transient diabetes insipidus during pregnancy: a clinical case and a review of the syndrome. Eur J Obstet Gynecol Reprod Biol. 2005;118:251-4.
80. Arima H, Wakabayashi T, Nagatani T, Fujii M, Hirakawa A, Murase T. Adipsia increases risk of death in patients with central diabetes insipidus. Endocr J. 2014;61(2):143-8.

Cite this article as: Abbas MW, Iqbal MA, Iqbal MN, Javaid R, Ashraf MA. Diabetes insipidus: the basic and clinical review. Int J Res Med Sci 2016;4:5-11.