

## Incidence of Urinary Malformations in Patients and Aged Forensic Samples in North East of Iran



Seyed Mohammad Hosseinipناه<sup>1\*</sup>, Heidar Tavilani<sup>2</sup>, Hamid Samavat<sup>3</sup> and Naghi Jabarivasal<sup>4</sup>

1. Department of Anatomy, Hamadan University of Medical Sciences, Iran
2. Department of Biochemistry, Hamadan University of Medical Sciences, Iran
3. Department of Medical Physics, Hamadan University of Medical Sciences, Iran
4. Department of Biophysics, Hamadan University of Medical Sciences, Iran

### Abstract :

Frequency of the urinary malformations(UM) in sample region of the country mirrors the important of regional causative problem. Khorasan is the largest province and has extended from north to south east of Iran. So the results of this research can be important. Silent and meanwhile progressive side effect of pollutions on human-being health is in great important. Hence here we report one of the congenital disorders which arises from risky enviromental conditions as UM. This research aims at studying the incidence of UM in the center of the largest province in Iran, *i.e.*, Mashhad. The study was done in two large hospitals naming "Imam Reza" and "Ghaem" in this city. Using retrospective foreground method in the first part of this statistical study, the researcher studied 774 cases of autopsies in pathological department of Ghaem Hospital from 1968 to 1992. Again using the same method, the researcher studied 4904 cases at urology department in Imam Reza hospital from 1985 to 1992. From 774 cases of autopsies, 33 cases were UM, and this made 4.26% of all the cases. Also, from these 33 cases, 69.2% were real polycystic of whom 88% were both sided and 12% were one sided polycystic.

From 4904 cases at urology department, 205 were UM; of which hypospadias was the main cause in nearly 76.9% of the cases and penile kind with subgroup of posterior penile was the cause of incidence of UM in 51.2%. At last, the statistical result obtained from this study was compared with the international ones. The difference was significant. This difference can be interpreted to be resulted from factors such as area conditions and others which will be discussed in the following sections in details.

**Key word :** Malformation, Urinary Tract, Forensic and North East of Iran.

### Introduction :

Khorasan is the largest province and has extended from north to south east of Iran. Its population is 6047661 or 1/10 of country and male to female ratio equal (3032701 male to 3014960 female) and area is 302966 km<sup>2</sup> or 1/3 of Iran. This province is near to Afghanistan and

Turkmenistan. Mashhad is the center of this province. Due to special religious situation, this city has good and big medical centers such as "Ghaem" and "Imam Reza" hospitals. Patients refer to these centers from different parts of this province and other provinces near to it (Iran Statistical Yearbook, 1998).

\* **Corresponding author :** Dr. Seyed Mohammad Hosseinipناه, Department of Anatomy, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran. Tel. : +98-811-8276295-8; FAX : +98-811-8276299; e-mail : hosseinipناه@hotmail.com

Urinary tract is composed of mesodermal layer (intermediate mesoderm) and endodermal layer (uretric bud) during embryonic and fetal periods. Congenital anomalies of urinary tract compare a diversity of abnormalities, ranging from complete absence to aberrant location, orientation and shape of different parts of urinary system as well as aberrations of the collecting system and blood supply. This wide range of anomalies results from a multiplicity of sequential and orderly manner. Abnormal maturation or inappropriate timing of these processes at critical points in development can produce any number of deviations in the development of urinary system. So this system makes an interesting field for basic and clinical researchs. On the other hand comparing these results with international statistical can guide to make programs for decreasing the causes.

### **Materials and Method :**

In part of this study retrospective foreground method was used for studying 774 cases at autopsies in pathological department of "Ghaem" Hospital from 1968 to 1992 about 24 years. From these, 33 cases were urinary malformations.

In another part of this study the same method was used again for studying 4904 cases at urology department in "Imam Reza" Hospital from 1985 to 1992 or 7 years. From these, 207 cases were urinary malformations.

### **Results :**

These results obtains from studying of figures 1 to 4.

**Polycystic Kidney :** From 774 cases of autopsies, 25 cases were polycystic

kidney disease and from these 22 cases were bilateral and 3 cases were unilateral. From bilateral cases, 20 cases were infantile and 2 cases were adult types (Fig. 1).

**Horseshoe Kidney :** In our research 2 of 33 cases of UM were horseshoe kidney (Fig. 1).

**Agenesis of kidney :** In autopsies, 2 cases were bilateral agenesis (Fig. 1).

**Uretropelvic Junction Obstruction:** Incidence of this malformation had been seen in 21 cases. Most of them had been discovered in patients after 20 years old (Fig. 1, 2, 3).

**Patent Urachus :** In this study only one case had this congenital anomalies (Fig. 1).

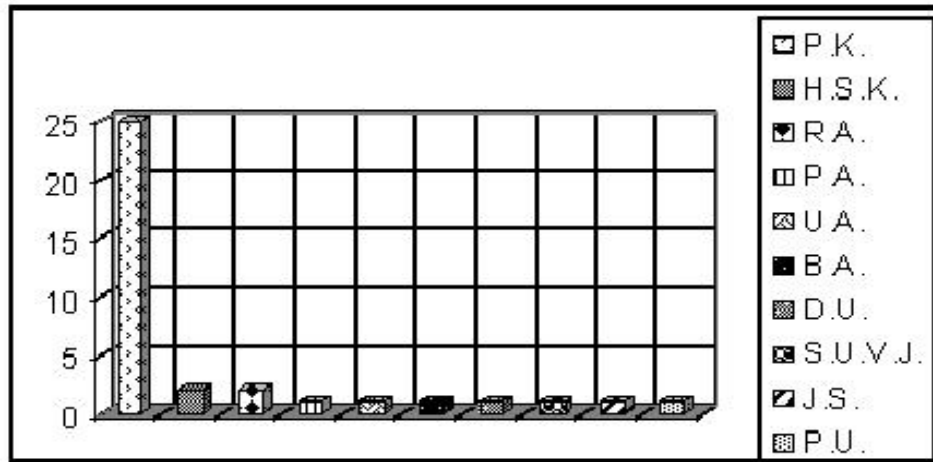
**Bladder Exstrophy :** Incidence of this UM was in 8 cases and male to female ratio was 3:1 (Fig. 2).

**Epispadias :** In our study there were 4 cases with this UM and male to female ratio was equal (Fig. 2).

**Hypospadiase :** This congenital anomalies form 2/3 of UM in patients. Most of these had occurred in posterior part of penis and had significant decrease in middle portion (Fig. 2, 4).

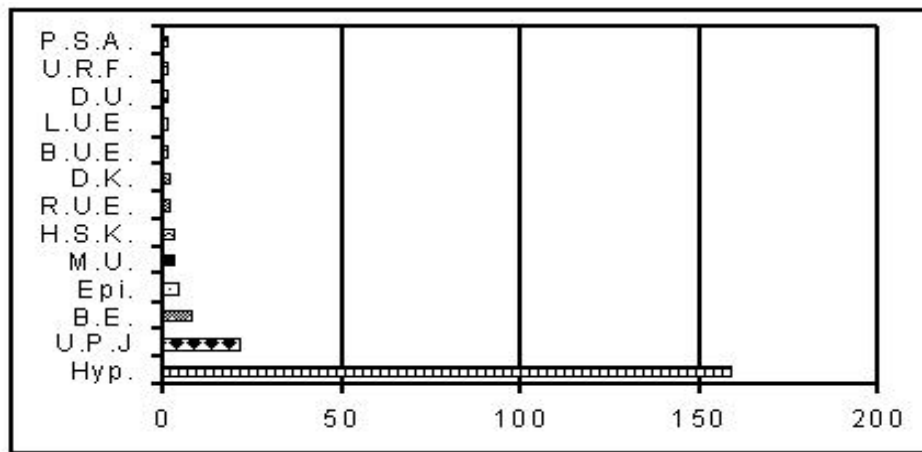
### **Discussion :**

**Cystic disease :** The kidney is one of the most common sites in the body for cysts. Although the lesions themselves in the various cystic conditions are histologically, similar that is microscopic or macroscopic sacs lined with epithelium- their number, location and clinical features are different.



**Fig 1 : Incidence of U.M in autopsies**

- |                            |  |
|----------------------------|--|
| P.K. = Polycystic Kidney   | H.S.K. = Horseshoe Kidney                      |
| R.A. = Renal Agenesis      | P.A. = Pelvis Agenesis                         |
| U.A. = Ureteral Agenesis   | B.A. = Bladder Agenesis                        |
| D.U. = Duplicated Urethra  | S.U.V.J. = Stenosis of Ureterovesical Junction |
| J.S. = Junctional Syndrome | P.U. = Patent Urachus                          |



**Fig 2 : Incidence of UM in patients**

- |                                 |                                 |
|---------------------------------|---------------------------------|
| P.S.A. = Penoscrotal Adhesion   | U.R.F. = Ureterorenal Fistula   |
| D.U. = Duplicated Urethra       | L.U.E. = Left Ureteral Ectopic  |
| B.U.E. = Biureteral Ectopic     | D.K. = Duplicated Kidney        |
| R.U.E. = Right Ureteral Ectopic | H.S.K. = Horseshoe Kidney       |
| M.U. = Megaureter               | Epi. = Epispiadias              |
| B.E. = Bladder Extrophy         | U.P.J. = Ureteropelvic Junction |
| Hyp. = Hypospadias              |                                 |

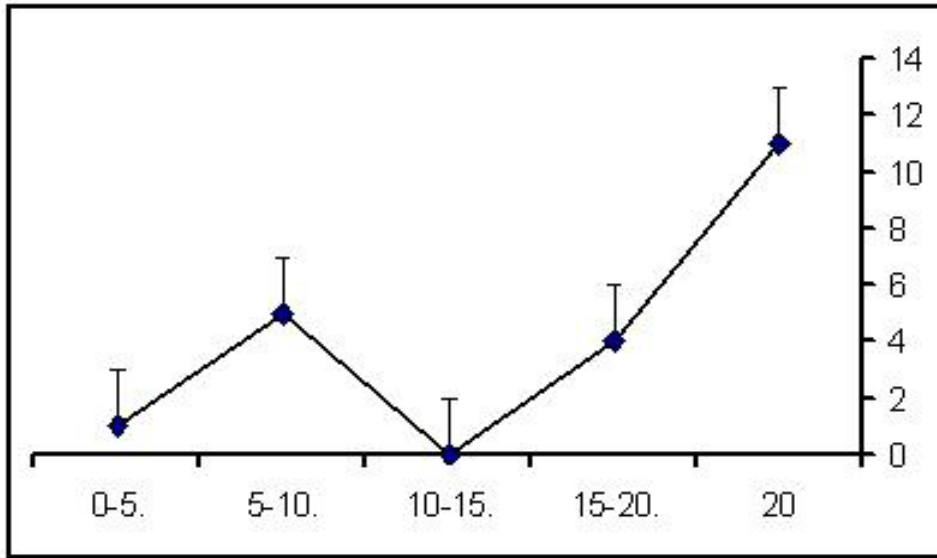


Fig 3 : Incidence of uteropelvic junction obstruction in different age groups of patients

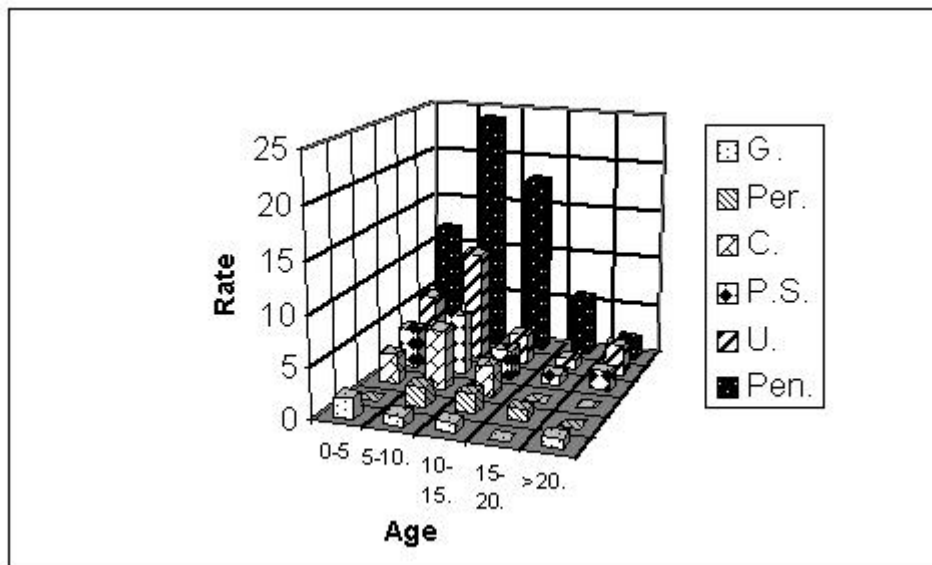


Fig. 4 : Incidence of hypospadias in patients.

G.	= Glandular	Per.	= Perineal
C.	= Coronal	P.S.	= Penoscrotal
U.	= Undifferentiated	Pen.	= Penile

**Autosomal Recessive (Infantile) Polycystic Kidney Disease :** When polycystic kidney disease is diagnosed in the neonate, it is most often of the recessive type (Cole *et al.*, 1987). The autosomal recessive type in the past has been referred to as the infantile form.

Autosomal recessive polycystic kidney disease (RPK) has been reported as a rare disease affecting about 1 in 40000 live births (Zerres *et al.*, 1988), as a not so rare disease occurring in 1 in 10000 in Finland (Kaariainen, 1987), or even as frequently as 1 in 5000 to 10000 (Berstein and Slovis, 1992).

However, as many as 50% of affected newborns die in the first few hours or days of life, making a significantly lower incidence among children alive after the age of 1 year. Of those infants who survive the neonatal period, approximately 50% are alive at 10 years of age (Kaplan *et al.*, 1989).

**Autosomal Dominant (Adult) Polycystic Kidney Disease :** The autosomal dominant form of polycystic kidney disease (DPK) is an important cause of renal failure, accounting for approximately 9% to 10% of patients in Europe and United States who receive chronic hemodialysis (7,8,9). Its incidence is approximately 1 in 500 to 1 in 1000, and approximately 500000 Americans (Gabow, 1993) have been diagnosed with the disease. Two genes for DPK have been localized, one on chromosome 16 (Reeders *et al.*, 1986) and one on chromosome 4 (Peters *et al.*, 1993).

In this study, from 774 cases of autopsies, 25 cases were polycystic kidney disease, which contains 69.2% of

malformations and 3.23% of all cases or 32 in 1000. From these 25 cases, 22 cases or 88% were bilateral and 3 cases or 12% were unilateral. From these 3 cases, one case was in left side and 2 cases were in right side. From bilateral cases, 45.5% was RPK and 4.5% was DPK. Therefore the DPK has meaningful increase more than 100 times.

**Horseshoe Kidney :** The horseshoe kidney is probably most common of all renal fusion anomalies. The anomaly consists of two distinct renal masses lying vertically on either side of the midline and connected at their respective lower poles by a parenchymatous or fibrous isthmus that crosses the midplane of the body. It was first recognized during an autopsy by Decarpi in 1521, but Botallo in 1564 presented the first extensive description and illustration of a horseshoe kidney. Horseshoe kidney occurs in 0.25% of the population, or about 1 in 400. As in other fusion anomalies, it is found more commonly in males by a 2:1 margin (Campbell, 1998).

In our research, there were 2 cases of 33 cases of anomalies or 0.26% of all autopsies or 26 in 10000.

**Bilateral Agenesis of the Kidney :** Of all anomalies of the upper urinary tract, bilateral renal agenesis (BRA) has the most profound effect on the individual. Although Wolfstrgel first recognized BRA in 1671, it was not until Potter's eloquent and extensive description of the constellation of associated defects that the full extent of the syndrome could be appreciated and easily recognized (Potter, 1946).

This anomaly is quite rare, with only slightly more than 500 cases cited in the literature. Potter estimated that BRA occurs once in 4800 births, but in British Columbia the incidence is 1 in 10000 births (Wilson and Baird, 1985). Davidson and Ross noted a 0.28% incidence in autopsies of infants and children, whereas Stroup and colleagues (Stroup *et al.*, 1990) detected an incidence of 3.5 per 100000 in the Center for Disease Control and prevention (CDC) Birth Defects Monitoring Program. As with most anomalies, there is a significant male predominance (nearly 75%).

There is a genetic predisposition to this syndrome with a high level of penetrance because when siblings and parents of an index child with BRA were screened, 4.5% had unilateral renal agenesis (Roodhooft *et al.*, 1984), and 3.5% had BRA (McPherson *et al.*, 1987).

In this study there were 2 cases of all autopsies or 26 in 10000. According to CDC research, there is significant increase, more than 100 times.

**Ureteropelvic Junction Obstruction :** Ureteropelvic Junction (UPJ) is seen in all pediatric age groups. At one point about 25% of cases were discovered within the first year of life, but today, with the widespread use of prenatal ultrasonographic imaging of fetuses, nearly all cases are discovered and diagnosed in the prenatal period (Brown *et al.*, 1987).

The obstruction occurs more commonly in males. Especially in the newborn period when the ratio exceeds 2:1 (Johnston *et al.*, 1977).

From all patients had admitted to urology ward, 21 cases had UPJ or 0.43%. From these 21 cases, 4.8% were discovered before 5 years old, 23.8% between 5-10 ages, 19% between 15-20 ages and 52.4% after 20 years old.

**Patent Urachus :** Congenital patent urachus is a lesion that is usually recognized in the neonate. It is a rare anomaly occurring in only three of more than 1 million admissions to a large pediatric center. The two forms of congenital patent urachus are (1) persistence of the patent urachus with a partially distended bladder and (2) a vesicumbilical fistula representing failure of the bladder to descend at all.

In a recent large series of urachal anomalies over a 25-year period, Cilento and colleagues found a patent urachus present in only 15% of patients (Cilento *et al.*, 1994).

In our study only one case was in all autopsies or 0.13%. This UM has significant decrease in this study.

**Bladder Exstrophy :** The incidence of bladder exstrophy has been estimated as being between one in 10000 and one in 50000 live births. However, data from the international clearing house for birth defects monitoring system estimated the incidence to be 3.3 cases in 100000 live births. The male to female ratio of bladder exstrophy derived from multiple series is 2.3:1. However, two series reported a 5:1 to 6:1 male to female ratio of exstrophy births (Ives *et al.*, 1980; Shapiro *et al.*, 1984).

The risk of recurrence of bladder exstrophy in a give family is

approximately one in 100. Shapiro and co-workers (Ives *et al.*, 1980) conducted a questionnaire of pediatric urologists and surgeons in North America and Europe and identified the recurrence of exstrophy and epispadias in only nine of approximately 2500 indexed cases.

Incidence of this UM was 0.16% and male to female ratio was 3:1 in our study.

**Epispadias :** In a combined study, Dees reported the incidence of complete epispadias to be one in 117000 males and one in 484000 females. The reported male to female ratio of epispadiase varies between 3:1 and 5:1 (Geahart and Jeffs, 1997).

In this study there was 4 or 8 cases in 10000 and male to female ratio was equal. The incidence of this UM is 40 times of wide world statistic.

**Hypospadias :** The incidence of hypospadias has been calculated as 1 in 300 live male births. In the United States, about 6000 boys with hypospadias are born each year (Duckett *et al.*, 1991).

But in this study there were 159 cases or 76.9% of UM. The incidence of hypospadias was 3.24% or 32 in 1000.

Then according to Welch, who estimated that 62% of the openings were subcoronal or penile, 22% were at the penoscrotal angle, and 16% were in the scrotum or perineum. Using the Barcat classification, Juskiewenski and colleagues reported that of 536 patients with hypospadias 71% of opening were anterior, 16% were in the middle, and 13% were posterior. Of the anterior group (383 patients), 13% were classified as balantic, 43% as subcoronal, and 38% as distal shaft.

The experience at the Children's Hospital of Philadelphia corresponds to these reports : 50% of openings were anterior, 30% were in the middle or midpenile and 20% were posterior. The anterior group was further classified as 19% glanular, 47% coronal and 34% distal shaft (Duckett and Snyder, 1992).

In our experience 46.5% of openings were anterior, 2.3% were in the middle and 51.2% were posterior. The anterior group was further classified as 10% glanular, 36.7% coronal and 53.3% anterior penile. The posterior group was further classified as 48.48% posterior penile, 40.9% penoscrotal and 10.62% perineal.

### **Conclusion :**

Research over the past years has revealed that numerous compounds present in our environment exert hormonal activity and thus have the potential to interfere with the endocrine system of humans and animals (Sohoni and Sumpter, 1998).

Today, we live in an environment where numerous types and large quantities of chemical substance exist, and their presence in our life is the inevitable price we pay for technological progress (Korner *et al.*, 1998).

Evidence accumulated indicates that the humans, domestic and wild life species have suffered adverse health consequences from exposure to environmental chemicals that interact with the endocrine system and so they are accurately called endocrine disrupting (Nagel *et al.*, 1998).

Endocrine disrupters pose the potential to modulate endocrine function

and thus adversely affect human urogenital development. Reported increases in incidences of certain cancers (breast, testis, prostate) may also be related to endocrine disruption (Lewis *et al.*, 2000; Welshons *et al.*, 1999). Because the endocrine system plays a critical role in normal growth, development and reproduction, even small disturbances in endocrine function may have profound and lasting effects. This is specially true, during highly sensitive prenatal periods that small changes in endocrine status may have delayed consequences that are evident much later in adult life or in a subsequent generation (Soto *et al.*, 1997).

Phytoestrogens are natural hormones present in many plants, and it, particularly has a high level in Soya. Several of the most potent known phytoestrogens belong to the group of isoflavonoids. The most frequently occurring isoflavonoids in food plants are genistein and daidzein. Other members of the flavonoid family, beside the isoflavonoid, exhibit estrogenic properties. The non-isoflavonoid flavonoids with estrogenic activity, designated flavo-estrogens, are widely distributed in food plants.

The researchers in the UK have found that sewage effluents, and in some cases rivers, were estrogenic, causing the production of vitellogenin (egg yolk protein) in male trout. Further research and fractionation of sewage effluents led to identification of estrone and 17 beta-estradiol as the main source of estrogenic activity in most effluents (Melnick *et al.* 2002). These two hormones are naturally excreted, in a conjugated form, in the

urine of women, bacteria in the sewage makes them re-activate the hormones (Legler *et al.*, 2002).

The fractionation research also detected ethinyl estradiol, from the contraceptive pill in some effluents, but the natural estrogens were always more important. It is important to mention that sewage effluents do also contain others estrogens, in particular alkyl phenols. It should be added that above-mentioned factors besides the flavonoids such as saffron, which is plentiful in Khorasan, province could bring about UM. In another step a research about the existence of endocrine disorders in the environment of this province is required.

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