

Relationship Between Post-Pubertal Mumps Infection In Males With Infertilityand Its Effect on The Result of Seminal Fluid Analysis and Occurrence of Immunological Infertility

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Abstract

Background: Mumps caused by paramyxovirus in the same group as parainfluenza and Newcastle disease virus, orchitis is the widely recognized complication in post-pubertal males. Approximately 50% of patients with orchitis have some degree of testicular atrophy, but sterility is rare.

Objective: To demonstrate the effect of the post-pubertal mumps infection on the result of seminal fluid analysis and to know if infection by mumps after puberty can lead to immunological infertility and production of anti-sperm antibodies.

Patients and Methods: Cross-sectional study in which 300 infertile males attending microbiology laboratory in Rizgary teaching hospital in Erbil city in Iraqi Kurdistan from November 2017- September 2018. Questionnaire was prepared for each male which included: name, age, occupation, history of mumps infection after puberty. Seminal fluid collected from each patient after 3 days of abstinence and analyzed according to WHO guidelines. Seminal fluid and serum obtained from each infertile male for the detection of anti-sperm antibodies by ELISA (enzyme-linked immunosorbent assay).

Results: The mean age of the participant in the study was (32.805 year) with the maximum and minimum age was (50, 18) years respectively. The incidence of post-pubertal mumps was (13.3%) and the incidence of abnormal seminal fluid analysis was (10%) and the highest abnormal seminal fluid variables among infertile males with post-pubertal mumps was oligoasthenozoospermia (43%) and the anti-sperm antibodies in the semen of infertile males with post-pubertal mumps infection was (60%) while the frequency of anti-sperm antibodies in the serum in infertile males with a history of post-pubertal mumps was (40%) which was higher than those with no history of post-pubertal mumps with highly significant relation statistically.

Conclusion: Abnormal seminal fluid analysis result may be due to post-pubertal mumps and it can lead to (Asthenozoospermia, Oligospermia, and Teratozoospermia). The highest percentage of abnormal seminal fluid variables was Oligoasthenozoospermia the occurrence of anti-sperm antibodies can be the sequence of post-pubertal mumps and by itself can lead to abnormality in the seminal fluid analysis. Mumps can lead to male infertility by affecting the seminal fluid parameters and also by the production of anti-sperm antibodies which can lead to subfertility in adult males.

Keywords: Paramyxovirus, post-pubertal mumps, anti-sperm antibodies

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Introduction

Mumps is an infectious viral disease that often results in painful swelling of the parotid gland. The virus is an RNA virus of the genus paramyxovirus which is disseminated from the human reservoir by direct contact, airborne droplets, fomites contaminated by saliva, and possibly by urine. The microbiological diagnosis is by serology or virus culture. Enzyme immunoassay for mumps immunoglobulin antibodies is most commonly utilized for detection of the virus. Antibodies (IgM) are detectable in the first few days of the ailment and are viewed as indicative. Likewise, seroconversion or a fourfold increment in IgG titer is additionally analytic [1].

The term 'mumps' gotten from an Old English verb meaning 'grimace', mirroring the impact of parotitis on facial expression [2]. The virus has no animal reservoirs and is simply a human illness. There is only one serotype of the virus, which can be moreover separated into 10-11 genotypes [3]. People always obtain long -life immunity when infected [4]. Complications of mumps comprise: orchitis, oophoritis, aseptic meningitis, encephalitis, deafness, pancreatitis, and at least one of these happen in up to 42% of patients with mumps [5], newly, there has been a resurgence in mumps orchitis, with epidemics being recorded every now and again [5,6].

In the pre-vaccine time mumps was described by between pandemic periods each 4–5 years

that most commonly affected children aged 5–7 years [7,8]. Internationally, 290 cases per year per 100 000 population were diagnosed between 1977 and 1985[9]. Since the introduction of the measles-mumps-rubella (MMR) vaccine in 1968, there has been a 99% decrease in the rate of the virus infection in the USA [10]. As of late, there has been a worldwide resurgence of mumps and ongoing episodes have primarily influenced youths and young adults [11].

Mumps orchitis recently seldom observe in children less than 10 years [12]. Orchitis is the most widely recognized complication of mumps in post-pubertal men, influencing about 20%-30% of cases [13] 10%-30% are bilateral [14].

Up to 30 - 40% of mumps infections are subclinical, and orchitis can occur without parotid involvement [15]. Recent data show that primary mumps infection among adults directly leads to infertility [16,17]. The consequence of the physiological events that occur between mumps virus primary infection and the development of infertility is not fully known [18]. It is not known whether mumps orchitis is purely a viral disease or a virus-induced immunopathological disorder [19]. There are reports that the mumps virus causes infertility without the involvement of orchitis [20] and they find many male infertility cases with decreased testosterone and a history of mumps infection and mild testicular pain during their mumps infection

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[21]. Anti-sperm antibodies have for the most part been found in homosexual males and in cases of testicular trauma, varicocele, mumps or orchitis, spinal cord injury, congenital absence of the vas and vasectomy [22].

Aims of this study are: to know the effect of the post-pubertal mumps infection on the result of seminal fluid analysis also to reveal if post-pubertal mumps infection can lead to immunological infertility and production of anti-sperm antibodies.

Patients and Methods

A cross-sectional study achieved in the microbiology laboratory in Rizgary teaching hospital in Erbil city/ Iraqi Kurdistan in the period from November 2017- September 2018. 300 infertile males were included in the study, a complete questioner form prepared for each person included: name, age, address, occupation, both medical and surgical history, and history of mumps and orchitis after puberty.

A semen specimen was collected after 3 days of abstinence period, in a wide -mouth, clean and sterile container, and each patient had been told to urinate before semen collection to decrease contamination of semen from debris or leukocyte. The seminal fluid specimens were collected masturbation after 3 days of abstinence and Semen analysis was performed following the standard procedures recommended by the World Health Organization (23).macroscopic and microscopic evaluation of the semen was performed within 30 minutes of liquefaction time after ejaculation at 37C and processed immediately after complete liquefaction. Following the liquefaction of semen, the wet sample was first analyzed by

putting 10µl of semen onto a glass slide and covered with a coverslip.

Around 200 spermatozoa in 5 fields at 40x magnification were counted for calculating the percentage of motility under four classes as the motility of each spermatozoon graded a, b, c, or d according to their motility.

- a- rapid progressive forward motility
- b- slow or sluggish motility
- c- non-progressive motility
- d- Immotile

Sperm counting was done by utilizing a modified Neubauer counting chamber after 1ml of semen diluted with 19 ml of buffer formal saline applied to the outer edges of the coverslip on each side of the chamber using the pasture pipette.

The sperm concentration and the total count were calculated in the following way: Counted sperm in five small squares X 20 dilution. Sperm morphology was studied on Papanicolaou stained smears, counting at least 200 spermatozoa utilizing 100 × magnification oil-immersing lenses. Sperm vitality was surveyed in wet mount smears after staining with Eosin. After the seminal fluid analysis was classified to normal and abnormal according to WHO guideline and then classified to different seminal fluid variables also according to WHO guidelines [32].Serum and semen collected from infertile males for detection of antisperm antibodies by utilizing ElISA (enzymelinked immunosorbent assay) used for detection ASAs in the serum and seminal fluid of infertile males qualitatively.

Statistical analysis

The data obtained in this study analyzed by using Microsoft Windows 10 and Excel

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program and SPSS(Statistical Package for the Social Sciences) version 23. The chi-squared test applied using the SPSS programming (version 23) to determine the relation between post-pubertal mumps infection and the occurrence of anti-sperm antibodies in the serum and seminal fluid, and P-value of < 0.05 was regard as the significance level

while the value <0.001 regarding highly significant (HS).

Results

This study shows that among 300 infertile males the incidence of males with of history post-pubertal mumps infection was 40 males which represent about (13.3%) as shown in Figure (1).

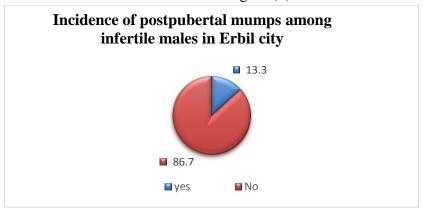


Figure (1): Incidence of post-pubertal mumps among infertile males

Table (1) shows that the result of seminal fluid variables among males with a history of mumps after puberty revealed that 10 (3.3%) were normal while 30 (10%) were abnormal

and the relation between seminal fluid analysis and history of mumps after puberty statistically was highly significant (P value= 0.0001).

Table (1): Relationship between result of seminal fluid analysis and history of post-pubertal mumps

			SFA		Total
			Normal SFA	Abnormal SFA	
History of	Yes	Count	10	30	40
mumps		% of Total	3.3%	10.0%	13.3%
	No	Count	148	112	260
		% of Total	49.3%	37.3%	86.7%
Total		Count	158	142	300
		% of Total	52.7%	47.3%	100.0%

*P value: 0.00

Table (2) which shows the relationship between the history of infection by mump after puberty with seminal fluid variables and this study that highest percentage of the seminal fluid variables shows that 32.5% of seminal fluid was oligoasthenozoospermia and the relation between the post-pubertal mumps infection with seminal fluid variables was statistically significant.

Table (2): Effect of post-pubertal mumps infection on seminal fluid variables

		Histor	ry of	Total	
		mumps			
			yes	No	
Result of	Normozoospermia	Count	10	148	158
SFA		%	25.0	56.9	52.7
	Asthenozoospermia	Count	5	37	42
		%	12.5	14.2	14.0
	oligo asthenozoospermia	Count	13	24	37
		%	32.5	9.2	12.3
	Oligoasthenteratospe	Count	4	15	19
		%	10.0	5.8	6.3
	Asthenoteratospermia	Count	3	10	13
		%	7.5	3.8	4.3
	Teratizoospermia	Count	3	13	16
		%	7.5	5.0	5.3
	oligospermia	Count	2	13	15
		%	5.0	5.0	5.0
Total		Count	40	260	300
	%	100.0	100	100	

^{*} P value: 0.000(HS)

Figure (2) demonstrated only abnormal seminal fluid variables in the infertile males with post-pubertal mumps, the distribution of abnormal seminal variable was as follow. Oligoasthenozoospermia (43%) followed by

asthenozoospermia(17%),oligoasthenoteratoz oospermia(13%),asthenoteratozoospermia and teratozoospermia(10%) and Oligospermia(7%).

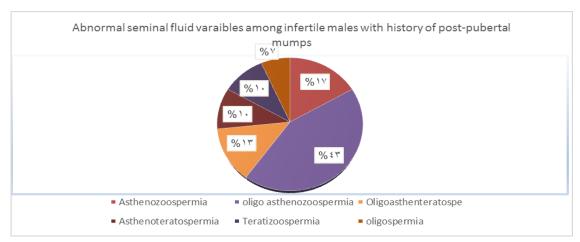


Figure (2): Abnormal seminal fluid variables among infertile males with post-pubertal mumps Table (3) revealed that the incidence of antisperm antibodies in the semen of males with a history of post-pubertal mumps infection was 24(60%) which higher than those they

didn't have a history of mumps after puberty (40%)with statically significant differences (0.02).

Table (3): Correlation between post-pubertal mumps infection and the occurrence of anti-sperm antibodies in the semen of infertile males

			ASA in semen		Total
			Negative	positive	
History of	yes	Count	16	24	40
mumps		%	40.0%	60.0%	100.0%
	No	Count	155	105	260
		%	59.6%	40.4%	100.0%
Total		Count	171	129	300
		%	57.0%	43.0%	100.0%

*P value: 0. 020(S)

Table (4) shows that the incidence of abnormal seminal fluid with anti-sperm antibodiesin semen 66(51.2%) which was higher than the normal result of SFS with

positive ASAs in semen, this relation was statistically non-significant (p-value: 0.49)(NS).

Table (4): Effect of anti-sperm antibodies on the result of seminal fluid analysis

			SFA		Total
			Normal SFA	Abnormal	
ASA in	Negativ	Count	95	76	171
semen	e	%	55.6%	44.4%	100.0%
	positive	Count	63	66	129
		%	48.8%	51.2%	100.0%
Total		Count	158	142	300
		%	52.7%	47.3%	100.0%

*P value: 0.29(NS)

Table(5) showed that the incidence of antisperm antibodies in serum in those they had a history of post-pubertal mumps 16(40%) which higher than the incidence of

ASAs in serum with no history of postpubertal mumps 47(18.1%) and this relation statistically was highly significant(P-value: 0.002).

Table (5): Correlation between history of post-pubertal mumps infection and the occurrence of antisperm antibodies in the serum of infertile males

			Serum	ASA	Total
			Negative	Positive	
History of	yes	Count	24	16	40
mumps		%	60.0	40.0	100.0
	No	Count	213	47	260
		%	81.9	18.1	100.0
Total		Count	237	63	300
		%	79.0	21.0	100.0

*P value: 0 .002(HS)

Table (6) shows that abnormal seminal fluid was higher among those with ASAs in serum was 38(26.8%) which was higher than the

normal result of seminal fluid analysis with positive ASAs in serum, this relation was statistically non-significant (P-value: 0.49).

Table (6): Correlation between ASAs in serum with the result of seminal fluid analysis

			Serur	n ASA	Total
			Negative	Positive	
	Normal SFA	Count	133	25	158
		%	84.2%	15.8%	100.0%
SFA	Abnormal	Count	104	38	142
		%	73.2%	26.8%	100.0%
Total		Count	237	63	300
		%	79.0%	21.0%	100.0%

*P value: 0.020(S)

Discussion

Mumps is a viral infections illness caused by the mumps virus, early signs and symptoms often include fever, muscle pain, headache, and poor appetite, feeling commonly unwell, this is then usually followed by painful swelling of one side or both sides of parotid salivary glands [24]. Manifestations of the disease are frequently more extreme in adults than in children, complications may include meningitis, pancreatitis, carditis, permanent deafness, and orchitis which can lead to male infertility[25].

Mumps virus has high tropism to the testis and may prompt male infertility. Sertoli cells are the significant focuses of Mumps virus infection. In any case, the mechanisms by which Mumps infection impairs male fertility and Sertoli cell function still not clear [26].

The result of this study revealed the incidence of post-pubertal mumps among infertile males in Erbil City was (13.3%) and this in agreement with a study done by (Niall et al) whom estimated that subfertility is occurred in 13% of mumps patients, and can occur in patients with no signs of testicular atrophy or orchitis [15]. Orchitis is viewed as the most well-known complication of mumps infection in the adult male. Orchitis usually

follows parotitis but may occur before or happen without parotid gland swelling.

Orchitis generally shows up during the primary seven days of parotitis, however, it can happen in the second or third week, and both side orchitis occurs less frequently (about 10% of cases) [27]. Also, our result was in agreement with a study by (Masarani et al) who stated that deterioration of fertility is predestined to happen in about 13% of patients with mumps orchitis may, and it can also can result in oligospermia, azoospermia, and asthenozoospermia (defects in sperm movement) [28].

Orchitis (testicular inflammation) is the most well-known complication in postpubertal males. In the pre-vaccine period, orchitis was manifest in 12% to 66% of postpubertal males infected with mumps. In 60% to 83% of males with mumps orchitis, just one testis was affected. Orchitis usually follows parotitis, but it may occur before it, begin at the same time, or it happens alone [29]. In this study, the result of seminal fluid variables among males with history of mumps after puberty revealed that 30 (10%) were abnormal and the relation between seminal fluid analysis and a history of mumps after puberty statistically was highly significant (P value= 0.0001) and this result

was lower than [30] which stated that 24% of adults had semen abnormalities.

This study demonstrated that there was a significant relationship between the result of seminal fluid analysis and the occurrence of post-pubertal mumps infection in which the abnormal seminal fluid was higher in those with a history of post-pubertal mumps than normal seminal fluid analysis and the percentage of abnormal seminal fluid variables follow was as Oligoasthenozoospermia (43%) followed by asthenozoospermia (17%),oligoasthenoteratozoospermia(13%), asthenoteratozoospermia and teratozoospermia(10%) while oligozoospermia was the lowest was Oligospermia (7%). The result of this study Oligoasthenozoospermia regarding was higher than those reported by (Cavallini) which was (12.4%),regarding asthenozoospermia, asthenoteratozoospermia and teratozoospermia was similar to our which result was(18.2%, 9.1%,9%) respectively while regarding Oligospermia our result was lower than reported by [31] which was (63.4%).

Oligoasthenoteratozoospermia is viewed as a serious variation from the norm related to the quality and amount of semen [29]. Men with severe oligoasthenoteratozoospermia have a decrease in the number of cells in their ejaculate, decreased total motility, minimum progressive forward motility, and a decrease in the number of sperms with normal morphology [32].

Our result was in agreement with a study done by [33] who showed that the semen analysis showed 100 % greatly reduced sperm count, and severe abnormalities in motility and morphology which confirms the mumps virus may be the possible reason for infertility in males with postbupertal mumps[33].

The prevalence of anti-sperm antibodies in infertile males with a history of post-pubertal mumps was higher than those with no history of post-pubertal mumps and the incidence of ASAs with abnormal SFA was higher than those with negative ASA in the semen.

The exact mechanism by which the mumps virus elicited anti-sperm antibodies is unknown, although animal models have shown that acute orchitis may be a causative factor in anti-sperm antibody production, towards sperm can prevent their motility via the female reproductive tract or prevent the procedure of fertilization [34].

Immunologic factors are considered as a significant reason for infertility [35]. One of the immunologic factors proposed for infertility is the presence of anti-sperm antibodies in serum. Anti-sperm antibodies are found in cervical mucus, seminal plasma and serum of men and women [36]. Immunity to sperm can be a result of infertility; humoral antibodies coordinated against sperm did not necessarily debilitate fertility unless the circulating antibodies are also found within the reproductive tract and on the living sperm surface [37].

Immunological infertility is thought to be the reason of infertility in 9-36% of the concerned couples. The main cause of immunological infertility is the production of anti-sperm antibodies (ASA), which influence the ability of fertilization of spermatozoa [38].

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ASA diminish the motility may of agglutination spermatozoa through and immobilization, thus preventing sperm movement through the female genital tract. A lowering in sperm motility has been seen by the different researchers as well in anti-sperm antibodies positive males [39].

The causal relation between mumps orchitis and anti-sperm antibodies has been indistinct, in spite of the fact that the antibodies were suspected to debilitate fertility, [Kalaydjiev et al.] shown that both the occurrence and the degree of serum antisperm antibodies among mumps orchitis patients were low, and did not bolster the theory of an enhanced humoral immunity towards spermatozoa[18].

In reports found that human seminal ASAs exert unwanted effects on sperm quality by changing important semen parameters, many paradoxical scientific papers exist; some of them emphasize that ASAs influence major semen parameters as specified by statistically significant differences in the semen parameters between ASA groups and fertile groups without ASAs as recordedrt4es by [40].

Conclusions

The post-pubertal mumps infection can influence the result of seminal fluid analysis and can result in abnormal seminal fluid analysis results. The production of anti-sperm antibodies can be the sequence of post-pubertal mumps and by itself can lead to abnormality in the seminal fluid analysis and mumps can lead to male infertility by affecting the seminal fluid parameters and also by the production of anti-sperm

antibodies which can lead to subfertility in the adult male.

Recommendations

Parents and communities ought to be made interested that neglecting to vaccinate their children undermines the future fertility of their children. Young men not immunized as kids ought to be directed and offered pressing immunization. We need more concentration on this virus and its relation with unexplained infertility because we have a small number of studies which concentrate on this issue.

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