

Public's knowledge regarding impact of advanced paternal age on offspring's health

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Abstract

Aim of Study: To assess knowledge of the population in Saudi Arabia about health hazards affecting the offspring of fathers with advanced age at the time of conception.

Methods: This is a nationwide study that included 1,218 adults living in Saudi Arabia. A study questionnaire was designed for online data collection using the "Google Forms".

Results: Almost half of participants were males (49.4%), age of 60.3% was 20-40 years, 22.2% were working in the health sector, while 34.4% were working in other sectors. The majority of participants (93.7%) were Saudi, and 52.7% were married. Only 19% stated that advanced paternal age is above 40 years, 54.4% were aware that aged mothers have more impact on their offspring's health, 73.3% considered that age at marriage is increasing in the community, while 85.5% considered that there is a need to raise the public's awareness about the baby's health problems associated with fathers' ageing. Only 12% of participants had poor knowledge about possible impact of advanced father's age on offspring's health. Participants' knowledge about impact of father's age on his offspring's health differed significantly according to their age, with those aged above 40 years having the least proportion of good knowledge (9.0%, $p=0.007$) and also differed with their employment status, with those employed at other than health sectors having the least proportion of good knowledge (7.6%, $p=0.001$).

Conclusions: The public in Saudi Arabia mostly have poor knowledge about impact of advanced paternal age on offspring's health. Most of them feel the need to raise their awareness about offspring's health problems associated with father's ageing. It is recommended to raise their awareness regarding the fact fathers, mostly after the age of 40 years, experience decreased fertility, and constitute a high risk for congenital malformations among their offspring. Couples must be counselled on the impact of advanced paternal and maternal ages on negative pregnancy outcomes and impaired offspring health.

Key words: Advanced paternal age, risk factors, congenital malformations, knowledge.

Introduction

For many years, advanced maternal age was blamed for the incidence of many syndromes among their offspring. This blame was based on strong evidence. However, the effect of advanced paternal age on offspring was not under focus, despite the increasing average paternal age (1).

There is no universally accepted definition for “advanced paternal age”, but father’s aged 40 years or older at the time of conception was frequently used (2). The possible impact of the relation between advanced father’s age and the incidence of health hazards among his offspring is not fully understood. Nevertheless, this may be attributed to new gene mutation secondary to the large number of self-deviations in spermatogenesis (3). Autosomal dominant mutations were estimated to be 0.5% among offspring of fathers aged older than 40 years (4).

In USA, the crude incidence rates for birth defects (per 10,000 births) among offspring of fathers with advanced paternal age were reported to vary according to type of birth defects, such as: anencephaly (1.21), spina bifida (3.32), encephalocele (0.75), ventricular septal defect (50.03), atrial septal defects (49.35), cleft lip with or without cleft palate (9.34), pyloric stenosis (13.71), craniosynostosis (5.35), gastroschisis (0.38), trisomy 21 (Down syndrome) 31.72, trisomy 13 (Patau syndrome) 0.90, and trisomy 18 (Edwards syndrome) 4.82 (5). However, no study has estimated prevalence of birth defects among offspring of fathers with advanced paternal age in the Kingdom of Saudi Arabia (KSA).

Other than birth defects, studies indicated that advanced paternal age is associated with 14% higher odds of premature birth, 18% of seizures, early childhood mortality (6), cerebral palsy (7) and some cancers, e.g., CNS neoplasms, acute lymphoblastic leukemia, acute myeloid leukemia (8). Therefore, impact of advanced paternal age at the time of conception on offspring is not negligible, and it might reach up to the risk of Down syndrome reported among 35-40-year-old mothers (9).

To the best of the researchers’ knowledge, no previous studies were conducted in KSA aiming to assess the association between advanced fathers’ age with health hazards among their offspring. Therefore, it is necessary to explore the public’s knowledge about this important health issue. Results of this study are expected to encourage healthcare planners toward educating the public to avoid the possible health hazards among offspring of fathers with advanced age.

Aim of study

To assess knowledge of the population in Saudi Arabia about health hazards affecting the offspring of fathers with advanced age at the time of conception.

Subjects and Methods

This research is a nationwide study that included adults (aged above 18 years) living in all 13 administrative regions of Saudi Arabia.

After thorough review of relevant literature, a study questionnaire was constructed by the researchers for data collection. It included two parts; the first part comprised personal characteristics (age, gender, educational status, employment, income and marital status), while the second part included 15 statements related to participants’ knowledge about the possible impact of advanced parents’ age on health of offspring. A pilot study was conducted on 50 participants. Test-retest reliability was assessed. In addition the internal consistency was evaluated using Cronbach’s alpha coefficient, which was 0.82. The questionnaire was then designed into online “Google Forms”.

A score of “1” was assigned to each correct response, while a score of “0” was assigned to each incorrect (or do not know) response. Scores of all responses were summed up to obtain participants’ total knowledge scores (with a minimum of 0 and a maximum of 15). Participants with total scores >8 were considered to have “Good Knowledge”, while participants whose knowledge scores were <7 were considered to have “Poor Knowledge”.

The minimum sample size was calculated using the Raosoft Sample Size Calculator Website (10), with 3% margin of error, 95% confidence level and 50% response distribution, to be 1,068. The study questionnaire was distributed according to a simple random sampling technique with proportional allocation to 1500 persons in all 13 Saudi Regions. However, only 1,218 responses were received (i.e., 81.2% response rate).

All data were cleaned for any duplication or incompleteness. The Excel spreadsheet data file was exported to the Statistical Package for Social Sciences (IBM, SPSS, version 25) file. Study variables were summarized and reported in terms of frequency distributions and percentages. All independent variables were compared across participants’ knowledge grades using the Chi-Square test. P-values <0.05 were considered statistically significant.

Participants’ data were kept confidential and were not used expect for research purposes. The ethical approval for conducting this study was obtained from the Institutional Review Board (IRB) in the Abha Maternity and Children Hospital, Saudi Ministry of Health.

Results

Table 1 shows that almost half of participants were males (49.4%). The age of 60.3% was 20-40 years. More than half of them (55.9%) were university educated. Approximately most one-fifth of participants (22.2%) were working in the health sector, while 34.4% were working in other sectors. The monthly income of 31.7% of participants' was 3,000-10,000 Saudi Riyals, while that of 39.8% was more than 10,000 Saudi Riyals. The majority of participants (93.7%) were Saudi, and 52.7% were married.

Table 2 shows that 36.8% of participants believed that advanced fathers' age is above 60 years, while 39.1% believe that it is above 50 years, while only 19% stated that it is above 40 years. More than half of participants (54.4%) were correctly aware that aged mothers have more impact on their offspring's health. Almost three-quarters of participants (73.3%) considered that age at marriage is increasing in the community, while 85.5% considered that there is a need for raising the public's awareness about offspring's health problems associated with father's ageing.

Table 3 shows that only 31.9% of participants correctly knew that advanced father's age affects his offspring's health. Regarding the association between father's aging and baby's morbidity, 19.2% knew its association with congenital heart disease, 12.2% knew its association with congenital hare lip, 25.2% knew its association with Down syndrome, 14.9% knew its association with congenital head deformities, 13.7% knew its association with epilepsy, 10.8% knew its association with cerebral palsy, 9.4% knew its association with brain tumors, 12% knew its association with blood diseases, and 20.4% knew its association with autism.

Figure 1 shows that only 12% of participants had good knowledge about possible impact of advanced father's age on offspring's health.

Table 4 shows that knowledge about impact of father's age on his offspring's health differed significantly according to participants' age, with those aged above 40 years having the least proportion of good knowledge (9.0%, $p=0.007$). Participants' knowledge also differed significantly according to their employment status, with those employed at other than health sectors having the least proportion of good knowledge (7.6%, $p=0.001$). However, participants' knowledge did not differ significantly according to their gender, educational status, monthly income, nationality or marital status.

Table 1: Personal characteristics of participants (n=1218)

Personal characteristics	No.	%
Gender		
• Male	602	49.4
• Female	616	50.6
Age group		
• <20 years	250	20.5
• 20-40 years	735	60.3
• > 40 years	233	19.1
Educational status		
• Primary/Intermediate	37	3.0
• Secondary	381	31.3
• University	681	55.9
• Postgraduate	119	9.8
Employment status		
• Unemployed	528	43.3
• Health sector	271	22.2
• Not health sector	419	34.4
Monthly income		
• <3000 SR	347	28.5
• 3000-10000 SR	386	31.7
• >10000 SR	485	39.8
Nationality		
• Saudi	1141	93.7
• Non-Saudi	77	6.3
Current marital status		
• Married	642	52.7
• Single	576	47.3

Table 2: Participants' knowledge regarding impact of parent's age on offspring's health

Knowledge statements	No.	%
Is age at marriage increasing in the community?		
• Yes	893	73.3
• No	182	14.9
• Do not know	143	11.7
At what age can fathers be considered as "advanced paternal age"?		
• >40 years	231	19.0
• >50 years	476	39.1
• >60 years	448	36.8
• Do not know	63	5.2
Which parent's age at conception has more impact on baby's health?		
• Mothers > fathers	662	54.4
• Fathers > mothers	28	2.3
• Both parents are equal	321	26.4
• Do not know	207	17.0
Is it necessary to raise public's awareness about possible hazards of conception associated with advanced paternal age?		
• Yes	1041	85.5
• No	54	4.4
• Do not know	123	10.1

Table 3: Participants' knowledge regarding impact of father's advanced age at conception on his offspring's health

Knowledge items	Yes		No		Do not know	
	No.	%	No.	%	No.	%
Does advanced father's age at conception affect his offspring's general health?	389	31.9	473	38.8	356	29.2
Does advanced age of fathers increase incidence of any of the following among offspring:						
• Congenital anomalies	285	23.4	450	36.9	483	39.7
• Congenital heart disease	234	19.2	415	34.1	569	46.7
• Congenital harelip	148	12.2	436	35.8	634	52.1
• Down syndrome	307	25.2	385	31.6	526	43.2
• Congenital head deformities	181	14.9	418	34.3	619	50.8
• Epilepsy	167	13.7	429	35.2	622	51.1
• Cerebral palsy	132	10.8	441	36.2	645	53.0
• Brain tumors	115	9.4	461	37.8	642	52.7
• Autism	248	20.4	390	32.0	580	47.6
• Blood diseases	146	12.0	443	36.4	629	51.6

Figure 1: Grades of participants' knowledge regarding impact of advanced father's age on his offspring's health

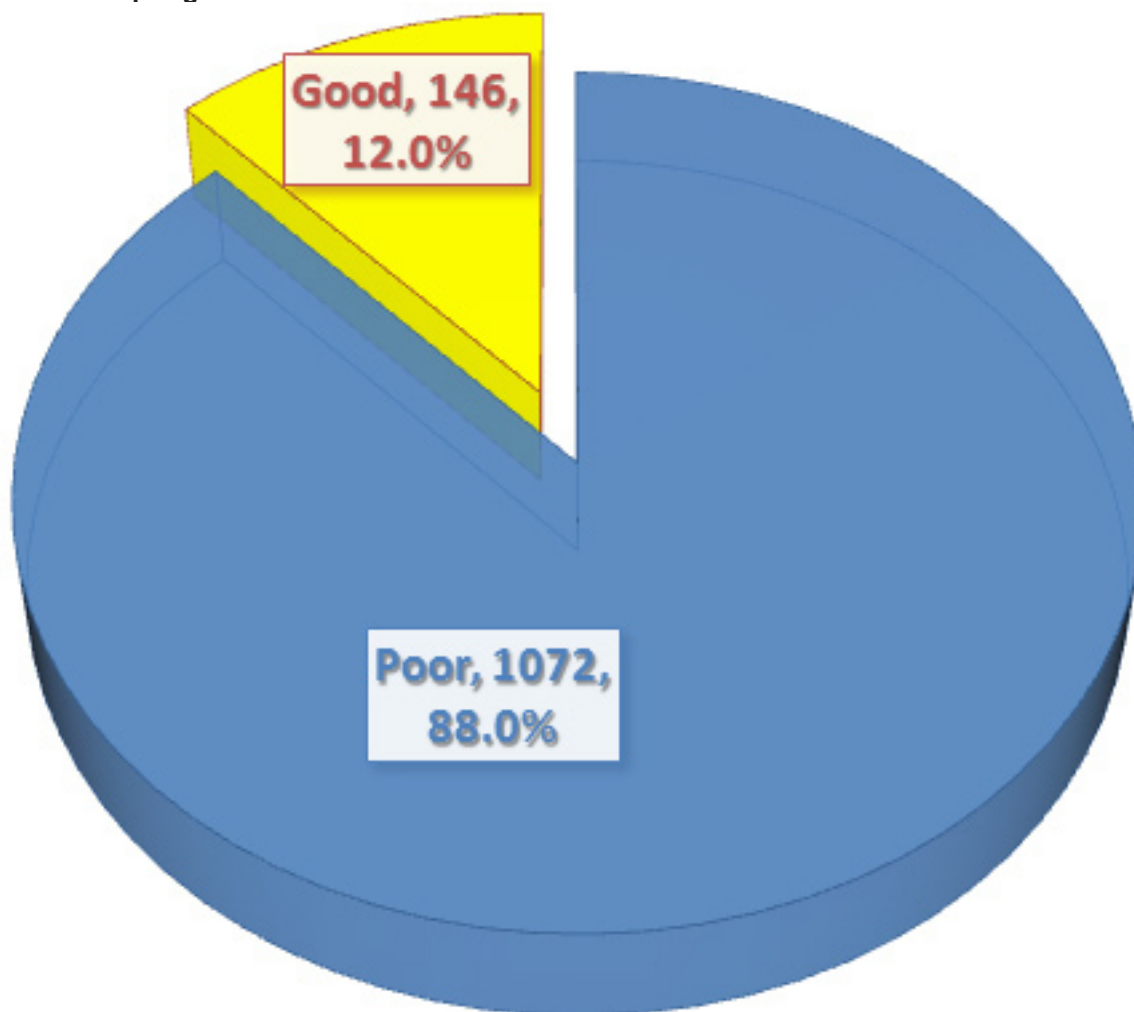


Table 4: Participants' knowledge regarding impact of advanced father's age on his offspring's health

Personal characteristics	Poor (n=1072)		Good (n=146)		P-value
	No.	%	No.	%	
Gender					
• Male	534	88.7	68	11.3	0.463
• Female	538	87.3	78	12.7	
Age group					
• <20 years	206	82.4	44	17.6	0.007§
• 20-40 years	654	89.0	81	11.0	
• > 40 years	212	91.0	21	9.0	
Educational status					
• Primary/Intermediate	33	89.2	4	10.8	0.221
• Secondary	329	86.4	52	13.6	
• University	610	89.6	71	10.4	
• Postgraduate	100	84.0	19	16.0	
Place of employment					
• Unemployed	461	87.3	67	12.7	0.001§
• The health sector	224	82.7	47	17.3	
• Not health sector	387	92.4	32	7.6	
Monthly income					
• <3000 SR	311	89.6	36	10.4	0.543
• 3000-10000 SR	338	87.6	48	12.4	
• >10000 SR	423	87.2	62	12.8	
Nationality					
• Saudi	1006	88.2	135	11.8	0.521
• Non-Saudi	66	85.7	11	14.3	
Current marital status					
• Married	573	89.3	69	10.7	0.160
• Single	499	86.6	77	13.4	

§ Statistically significant

Discussion

There is a consistent increase in average paternal age across all races, ethnicities, and regions, and regardless of level of education in several countries (11-12). Similarly, there are changes in Saudi Arabian families due to rising age at marriage and cultural or economic pressures (13). In the current era, when childbearing is often being delayed, there has been great focus on the effects of advanced maternal age on pregnancy and beyond, while the discussion of advanced paternal age has taken a backseat (14).

Our study revealed that the majority of participants had poor knowledge regarding the impact of fathers' age at conception on their offspring's health. Almost three-quarters of participants considered that age at marriage is increasing in the community, while only 19% of participants stated that it is above 40 years and more than half of participants were aware that aged mothers have more impact on baby's health. Most participants felt the need for raising the public's awareness about baby's health problems associated with father's ageing at conception.

Ford et al. (15) noted that natural fertility rates decline with men older than 40 years compared with men younger than 30 years. After controlling for maternal age, Hassan et al. (16) reported that 76.8% of men younger than 25 years impregnated their female partners within 6 months compared with 52.9% of men older than 45 years. Moreover, advanced paternal age has been linked to increased rates of miscarriage. After controlling for maternal age, partners of men older than 35 years were more likely to miscarry than partners of men younger than 35 years (17-18).

Brandt et al. (19) stated that DNA fragmentation is independently associated with infertility and lower livebirth rates. Therefore, it has been suggested that DNA fragmentation should be part of the routine evaluation of sperm quality for couples undergoing assisted reproductive technologies with advanced age husbands (20).

It is to be noted that most professional societies, including the American College of Obstetrics and Gynecology, the National Society of Genetic Counselors, and the International Society of Prenatal Diagnosis, have not published formal practice guidelines on advanced parental age (19). Ramasamy et al. (21) argued that advanced maternal age is considered at the age of 35 years, and the likelihood of pregnancy declines after intercourse with men aged >34 years (22). However, the American College of Medical Genetics has defined advanced parental age as 40 years or older at the time of conception (19).

About one-third of participants in our study indicated that advanced paternal age may negatively affect baby's health, with higher incidence of congenital heart diseases (19.2%), harelip (12.2%), Down syndrome (25.2%), congenital head deformities (14.9%), epilepsy (13.7%), cerebral palsy (10.8%), brain tumors (9.4%), blood diseases (12%), or autism (20.4%).

Several studies confirmed that advanced paternal age at conception constitutes a significant risk factor for high morbidity outcome among offspring. Archer et al. (5) reported high incidence rates for congenital malformations among offspring of fathers with advanced paternal age, e.g., anencephaly, spina bifida, encephalocele, ventricular septal defect, atrial septal defects, harelip, cleft palate, and Down syndrome.

Malaspina et al. (23) reported that, in a subgroup of men 40-49 years old, the relative risk of developing autism spectrum disorders was six-fold more likely in their children than the offspring of men younger than 20 years of age. Toriello and Meck (24) found that, either alone or in combination with a maternal age effect, advanced paternal age may increase the risk of Down syndrome. Khandwala et al. (12) added that advanced paternal age was associated with an increased risk of premature birth, low birth weight, and low Apgar score.

Moreover, advanced paternal age was reported to be a risk factor for several birth defects. Odds ratios (OR) more than 1 were reported with each year of increase in paternal age for cleft lip (OR: 1.02), diaphragmatic hernia (OR: 1.04), right ventricular outflow tract obstruction, (OR: 1.03), and pulmonary stenosis (OR: 1.02) with each year of increase in paternal age (25). Although these odds suggest a small magnitude of, the cumulative risk over decades is substantial. A 40-year-old father would have twice the odds of having a child with diaphragmatic hernia compared with a 20-year-old father given the adjusted OR of 1.04. The relative risk for offspring with schizophrenia was 2 for fathers aged 45-49 years and 3 for fathers aged >50 years Malaspina et al. (26).

Johnson et al. (27) explained the high morbidity rates among offspring of fathers with advanced age by that increasing paternal age negatively affects sperm quality, with decline in semen volume, total sperm count and motility, percentage of morphologically normal sperm, and increased DNA fragmentation rates. These age-dependent changes in semen quality could be attributed to normal physiological changes in the reproductive tract that occur with ageing, decreased capacity for cellular and tissue repair of damage induced by exposure to toxicants or diseases, and increased chances with age of having reproductive damage resulting from exogenous exposures such as smoking or infections (28). However, the fact that both normal physiological processes and environmental factors could be held responsible for the effects of ageing on the male reproductive system adds to its complexity (29).

The present study revealed that public's poor knowledge regarding the possible impact of advanced paternal age on offspring's health is quite general, as participants' knowledge did not differ significantly according to their gender, educational status, monthly income, nationality or marital status. However, participants' knowledge grades differed significantly according to their age and employment status, with those aged above 40 years and

those with other than health sectors employment having the least proportion of good knowledge, while younger participants (aged less than 20 years) and those employed in the health sector, despite having high percentages of poor knowledge, had relatively the highest percentages of good knowledge.

Although it is alarming that the majority of participants had poor knowledge about the negative impact of advanced paternal age on offspring, it is not surprising that those employed in the health sector had relatively less percentage of poor knowledge. Moreover, higher percentage of poor knowledge among older participants may be attributed to the fact that internet sources of knowledge are more frequently used by younger people. However, the present study indicates that it is a pressing necessity to raise the awareness of the public in Saudi Arabia regarding the fact that not only mothers, but also fathers at a given point in time, mostly after the age of 40 years, experience decreased fertility, and constitute a high risk for congenital malformations among their offspring.

Demographic studies have revealed that the number of births to parents older than 35 years has more than doubled in the past 20 years in the USA. This increase in parental age is a public health concern since more infants are being born with increasing risk for genetic abnormalities (30).

Societal pressures are partly to blame for delaying childbearing and the rising age of parents at conception. Careers and educational aspirations, along with an increased life expectancy and the nearly ubiquitous use of contraception, have decreased accidental birth rates and increased parental age at first childbirth. Moreover, the success of in vitro fertilization has given many couples a type of 'reproductive security blanket' by assuring them that if the traditional methods of achieving conception are not successful, technology will come to their rescue (31). Additionally, increased rates of divorce and remarriage, resulting in many fathers having a child with a second spouse or partner later in life, has contributed to increasing paternal age. Improved methodologies for assisted reproductive technologies have paralleled these lifestyle and cultural changes, allowing for couples to start families later in life despite declining fertility (32).

Brandt et al. (19) advocated that raising the awareness of couples regarding the risk of advanced paternal age on their offspring should be performed by offering preconception genetic counseling. Given that maternal and paternal ages are highly correlated, many couples may already be presenting for genetic counseling to discuss maternal risks and their pregnancies. Moreover, Durairajanayagam (33) stressed that couples must be counselled with equal emphasis on the contribution of both advanced paternal and maternal ages as being potential risk factors of negative pregnancy outcomes and impaired offspring health. In that respect, the public's awareness and recognition of the possible impact of risk factors present in daily life is crucial amongst couples seeking conception.

In conclusion, the public in Saudi Arabia mostly have poor knowledge about impact of advanced paternal age on offspring's health. Their poor knowledge is less among younger people and those who work in the health sector. Most of them feel the need to raise their awareness about offspring's health problems associated with father's ageing. Therefore, it is recommended to raise the awareness of the public in Saudi Arabia regarding the fact fathers, mostly after the age of 40 years, experience decreased fertility, and constitute a high risk for congenital malformations among their offspring. Moreover, couples must be counselled on the impact of advanced paternal and maternal ages on negative pregnancy outcomes and impaired offspring health.

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