In Vitro Fertilization Informed Consent: Revisited, Empirically

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ABSTRACT **Background:** A thorough informed consent (IC) process is required before in vitro fertilization (IVF) treatments can begin because these treatments are by and large elective and they have expectable and preventable complications, such as ovarian hyper-stimulation syndrome and multi-fetal pregnancies.

Objectives: To empirically examine whether patient knowledge and understanding of potential hazards associated with IVF treatment are better after the IC process compared to before. The authors hypothesized that patients' better understanding of potential complications would be translated and expressed as rational choices of treatment alternatives.

Methods: Responses of 48 IVF patients after IC process (study group) from two IVF units in northern Israel were compared to those of 46 patients before IVF (control group).

Only women undergoing IVF for first time who were older than 18 years of age were eligible for the study.

Results: Socio-demographic parameters were found to be quite similar between the study group and the control group. Contrary to our expectations, in the study group 12 women (25.5%) considered delivery of a single baby as their optimal result, compared to 15 (32.6%) in the control group. Furthermore, preferences shifted toward triplets: eight patients (17%) after IC considered this option as their best result, compared to only five patients (11%) before IC.

Conclusions: IC process goals are not achieved under current practices, at least as far as IVF treatment are concerned. New tools and incentives should be implemented to meet the requirements dictated by the laws regarding patient rights.

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In the State of Israel the Law of Patient rights dictates that no clinical treatment will be performed unless informed consent (IC) for the procedure has been given. Furthermore, the attending physician is required to deliver relevant information in a reasonable fashion to enable patients to decide whether they accept the suggested treatment after considering the advantages and disadvantages to all relevant alternatives [1].

The question whether these directives are met, using in vitro fertilization (IVF) treatments as a case study, was examined in a previous study. Results were, by and large, disappointing: The informed consent forms for IVF and embryo transfer (ET) that are currently being used were found to be fundamentally inaccurate and outdated. In some cases, information such as the number of embryos to be transferred is grossly obscured. The conclusion of that study was that upgrading of the consent forms is urgently needed. New versions should clearly distinguish between common and controllable complications vs. uncommon uncontrollable ones [2]. The purpose of the current study was, therefore, to re-examine the same question, this time empirically.

The importance of the present study is twofold. First is social/ethical, and the second is clinical. The social/ethical question, using IVF as a case study, addresses whether patients really understand treatment options as well as potential risks and benefits. Do patients really execute their power to chose the treatment when there are high prospects of success (i.e., take home a healthy baby) and low risks of complications (i.e., ovarian hyper-stimulation syndrome) [3]?

The clinical issues also have concerns: both personal and public. The personal perspective is that treated couples obviously expect to be able to take home a healthy baby. In many cases this is the result. In some cases, however, the short-lived happiness of being pregnant may be replaced by weeks of uncertainty after the birth of a very low birth weight (VLBW) infant being treated in the neonatal intensive care unit (NICU), which is later replaced by understanding that they are going to have a child with disabilities who will never be independent and will need some kind of support for life [4].

The public perspective is that local statistics show that about a quarter of the very low birth weight infants in Israel are the result of preterm labor, commonly associated with multi-fetal pregnancy after fertility treatments, mainly IVF [5]. NICUs in Israel are overcrowded and understaffed with a cross-infection rate three time higher than that of other Western countries [6].

PATIENTS AND METHODS

Participants in the study were IVF patients in two public hospitals in northern Israel. The study design was approved by Hel-

sinki committees at both institutions.

Participants were interviewed using a semi-open questionnaire to define their knowledge and understanding of:

- The chances of having a multi-fetal pregnancy (MFP), as a result of the treatment
- The relationship between MFP and the chances of having pre-term labor (PTL)
- The relationship between PTL and pre-mature, VLBW infant with associated complications

The study evaluated in vitro fertilization (IVF) patient responses to the questionnaire before and after the informed consent process. Only women who underwent IVF for the first time and who were at least 18 years old were eligible to participate.

PARTICIPANTS

The participants of the study were two separate groups of patients. The intervention group included patients after meeting to discuss the process of IVF before their first treatment (intervention group). The explanation about the treatment was given by the staff of the IVF unit based on the Israeli informed consent document for IVF and ET [7]. The IVF-IC process was the standard procedure of the participating medical staff. The researchers were not present during the process so that they did not influence its content and quality.

The control group included patients before the process of participating in their IC as part of the treatment.

The study was designed to include a study group and a control group, rather than interviewing the same group of patients before and after the procedure. It seemed plausible that patients interviewed before IC would be more attentive during the process, leading to a bias toward a better effect than what actually occurred.

The investigators had no influence on either the process or the patients. The process of accepting patients' IC for the treatment was similar in both units. Patients were interviewed within 3 weeks of getting their IC to the treatment of IVF and ET. Participant were interviewed by two trained female interviewers either in Hebrew or Arabic, according to the preference of the patient.

Sample size was based on the results of similar studies in related clinical areas [8]. It was assumed that the proportion of correct answers in the informed (intervention) group would be at least 70%, compared to 40% or less in the un-informed (control) group. The effect was expected to be noticed concerning, both desired (i.e., intra-uterine singleton pregnancy) and undesired results (e.g., multi-fetal pregnancy).

To reach a level of statistical significance of 5% and power of 80%, a sample size of 42 women in each group was required.

We initially approached 60 couples for each study group to compensate for cases that would not meet inclusion criteria or would decline participation.

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software (SPSS, IBM Corp, Armonk, NY, USA).

Table 1. Study population

	Group 1 - Before	Group 2 - After	*P* value
Average age, years ± SD	31.9 ± 6	30.1 ± 7	0.2
Country of origin			
Israel	39 (85%)	38 (79%)	0.5
Former Soviet Union	6 (13%)	9 (18%)	
Other	1 (2%)	1 (2%)	
Religion			
Jewish	24 (52%)	26 (54%)	0.4
Christian	1 (2%)	4 (8%)	
Muslim	16 (35%)	17 (35%)	
Druze	5 (11%)	1 (2%)	
Marital status			
Single	9 (19.6%)	4 (8.3%)	0.8
Married	33 (71.7%)	42 (87.5%)	
Divorced	2 (4.3%)	2 (4.2%)	
Widow	2(4.3%)	0 (0%)	
Education			
Elementary	2 (4.3%)	2 (4.2%)	0.2
High school	21 (45.7%)	24 (53.3%)	
College/university	23 (50.0%)	19 (42.2%)	

RESULTS

In the intervention group nine women declined and three did not meet the inclusion criteria. The final study group included 48 patients (84%). In the control group, 11 women declined and three did not meet the inclusion criteria. The final control group included 46 patients (80%).

The study group and the control group were found to be similar in their socio-demographic characteristics. Average age was 30–32 years old, respectively. The majority (79–85%) were born in Israel. About a half (54–52%) were Jewish, and about a third (35–35%) were Moslem (more than the proportion of this sector in Israel, which is about 20%). Others were Christians (2–8%) and Druze (2–11%).

Education was examined as a proxy variable of socioeconomic status. About 95% of participants in both groups had either a high school or college education [Table 1].

BEST RESULT OF IVF TREATMENT

In the study group (after IC) 12 women (25.5%) considered delivery of a single baby as their optimal result, compared to 15 (32.6%) in the control group (before IC). The difference was statistically significant ($P = 0.02$) in the negative direction, that is fewer patients after IC thought that a single baby is the best result, than before IC. Furthermore, paradoxically, preferences shifted toward triplets: 8 patients (17%) after IC considered this option as their best result, compared to only 5 patients (11%) before IC.

KNOWLEDGE ABOUT COMPLICATIONS OF MFP

Patient knowledge about the risks associated with MFP was evaluated by a series of nine multiple choice questions concerning common complications such as pre-term labor, low birth weight, and caesarian section rate.

The level of knowledge about complications of MFP before the IC process was 51%, which was higher than expected. We expected 40%. However, the level of knowledge about complications of MFP after the IC process was only marginally changed 57%, much less than expected (70%), and with no statistical significance ($P = 0.5$) compared to the control group.

NUMBER OF EMBRYOS TO BE TRANSFERRED

Paradoxically again, after IC, no woman in the study group wanted to have a single embryo transfer, compared to 5 (11.9%) in the control group (before IC). Furthermore, 26 women (56.5%) in the study group wanted to transfer three or more embryos compared to 14 (33.3%) in the control group. Both results were statistically significant ($P = 0.02$, $P = 0.03$, respectively).

DISCUSSION

The frustrating question of what does informed consent mean and why are its goals imperfectly realized was asked by Cassileth and his colleagues almost 40 years ago. [9]. Obviously, it is frustrating is to realize that this question is still relevant today. [10] Levitt and Dubner, authors of *Super-freakonomics* [Hebrew] asserted that people react to incentives. We agree with their assessment [11]. In Israel, compensation to patients who experience undesired results from medical procedures is dependent on their ability to prove negligence on behalf of their attending physician. A physician's interest may be self-defense. IC processes and forms are geared to protect the physician in case something goes wrong, rather than to empower patients in the decision making process of diagnosis and treatment. This finding was the conclusion of the first theoretical study and is the conclusion of our current empirical study.

This situation is not unsolvable. In fact the solution is well recognized and established in several countries [12].

CONCLUSIONS

The results of this study are a call for action. Policymakers are urgently requested to consider a comprehensive remake of the informed consent process, at least before IVF, to develop such an informed consent document that more closely fulfills its ethical and juristic goals.

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It is not in the stars to hold our destiny, but in ourselves.
William Shakespeare (1564–1616), British playwright, poet

It is better to fail in originality than to succeed in imitation.
Herman Melville (1819–1891), American novelist, short story writer, essayist, and poet