To estimate the cost of diagnosis of infertility and its management including In Vitro Fertilization and quality of life among Infertile couples

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List of Abbreviations

Abbreviation	Full Form
AB-PM-JAY	Ayushman Bharat- Pradhan Mantri Jan Arogya Yojana
ART	Assisted Reproductive Technology
CC	Clomiphene Citrate
CGHS	Central Government Health Scheme
CHSI	Costing of Health Services in India
DHC	Direct Health Costs
DHR	Department of Health Research
EQ-5D	EuroQol - 5 Dimensions
ET	Embryo Transfer
GnRH	Gonadotropin-Releasing Hormone
HCG	Human Chorionic Gonadotropin
HR	Human Resources
HRQoL	Health Related Quality of Life
HTAIn	Health Technology Assessment in India
IC	Indirect Costs
ICMR-NIRRCH	Indian Council of Medical Research-National Institute of Research in Reproductive and Child Health
ICSI	Intracytoplasmic Sperm Injection
INR	Indian Rupee
IQR	Inter-Quartile Range
IUI	Intra-Uterine Insemination
IVF	In Vitro Fertilization
JNMC	Jawaharlal Nehru Medical College
LH	Luteinizing Hormone
MAMC	Maulana Azad Medical College
NMC	Non-Medical Costs
OHSS	Ovarian Hyperstimulation Syndrome
OOPE	Out-of-pocket Expenditure
OPU	Ovum Pickup
PCOS	Polycystic Ovarian Syndrome
PGIMER	Post Graduate Institute of Medical Education and Research
PIS	Participant Information Sheet
SAT	SAT Hospital, Govt. Medical College, Trivandrum
SRIHER	Sri Ramachandra Institute of Higher Education and Research
USG	Ultrasonography
VAS	Visual Analogue Scale
WHO	World Health Organization

Contents

Table of Contents

List of Tables

List of Figures

Executive Summary

The World Health Organization (WHO) reports that primary infertility affects 3.9-16.8% of couples in India. Despite its prevalence, infertility gets inadequate attention in India's public health agenda, leading to limited coverage for diagnosis and treatment under national health initiatives. Challenges include inadequate infrastructure, trained personnel, and high treatment costs. Female factors contribute to 46% of infertility cases, while male factors contribute to 20%. About 8% of infertile couples require advanced treatments like In vitro Fertilisation (IVF), which are expensive and technically demanding. IVF involves several steps, including ovarian stimulation, egg retrieval, fertilization, embryo transfer, and monitoring for pregnancy. Different stimulation protocols are used, with GnRH antagonist protocols being common due to lower risks. IVF carries risks such as ovarian hyperstimulation syndrome and complications from egg retrieval. Public ART services are limited, leading to reliance on expensive private providers. Regulatory frameworks exist, but prices remain uncontrolled, causing financial strain on couples. Efforts are being made to include IVF in government health schemes like Pradhan Mantri- Jan Arogya Yojana (PM-JAY), necessitating cost assessments. In response to this interest shown by the user department (NHA), HTAIn DHR allocated this study to HTA Resource Hub at ICMR NIRRCH, Mumbai. This study aimed to estimate cost of diagnosis of infertility and its management including in vitro fertilization and quality of life among infertile couples.

Our objectives were to estimate health system costs of diagnosis and treatment of infertility including IVF, to estimate Out-of-pocket expenditure incurred by infertile couples including IVF services and to assess quality of life among couples accessing services for diagnosis and treatment of infertility including IVF. We identified three public and two private tertiary health facilities that were willing to participate in the study. Primary data was collected from 30 patients undergoing IVF treatment and 100 patients undergoing infertility treatment (particularly diagnosed with single cause such as PCOS, endometriosis, tubal factor, uterine factor and male infertility) at each site along with health system costing.

Among couples undergoing IVF treatment, oligospermia and tubal factor infertility were the leading cause of infertility.

Health related quality of life (HRQoL) of these patients was assessed using five-dimensional Euro-QoL questionnaire (EQ-5D-5L) and Visual Analogue Scale (VAS). The quality-of-life measures for couples undergoing IVF was slightly reduced compared to the ones who were not receiving IVF. Pain/discomfort and Anxiety/depression contributed to poor quality of life in wives while husbands had poor scores in the dimension of anxiety/depression.

The average Out-of-Pocket Expenditure (OOPE) of participants undergoing IVF treatment was Rs. 1,09,671 and Rs. 2,30,668.5 for one IVF cycle at public and private hospitals respectively. 88.5% of patients undergoing IVF had incurred catastrophic expenditures due to the treatment.

The cost of providing one IVF cycle was estimated from the data collected from the relevant cost-centres of the hospitals. A mixed method costing analysis was done using primary data from a health system’s perspective. The health system cost of providing one IVF cycle including costs of medicines irrespective of the facility's operational efficiency (pertaining to number of IVF procedures done in one year) was estimated to be Rs. 81,332 (+/- 12,849).

Among couples undergoing infertility treatment, PCOS was the most common factor of infertility among the five factors considered. The median out-of-pocket expenditure for infertility treatment was Rs.11317 (IQR: 4801, 19513). Although direct medical costs for medicines and investigations were high in private facilities, the non-medical and indirect costs were higher among those seeking infertility services from public facilities. About 25% patients undergoing infertility treatment incurred catastrophic expenditure due to the treatment. Patients with uterine factor infertility and endometriosis had the lowest Health-Related Quality of Life. Pain/discomfort and anxiety/depression were the dimensions contributing most to the poor quality of life of the patients. The health system cost of infertility management for one year in the public facilities ranged between Rs. 6,822 to Rs. 11,075 which was found to be higher in the private than public facilities.

Recommendations from this study:

- Based on study findings, the IVF package for consideration under Pradhan Mantri Jan Arogya Yojana (PM-JAY) could be considered at Rs. 81,332 for one IVF cycle.
- Currently, OPD expenses are not covered under PM-JAY. As the majority of expenditure for infertility treatment including IVF is OPD based, this consideration needs to be made for including IVF in the PM-JAY package.
- Since 25% of couples undergoing infertility treatment face catastrophic expenditure, this cost could also be considered for reimbursement under PM-JAY.

Chapter 1: Introduction

According to the World Health Organization (WHO), the overall prevalence of primary infertility in India ranges from 3.9-16.8% [(1)]. Although infertility is one of the important reproductive health problems increasingly faced by couples in India it still does not feature on the public health agenda in India. Diagnosis and treatment of infertility is not prioritised in the national health mission and RMNCH+A program. Thus, these services are rarely covered through public health financing. Availability, access, and quality of interventions to address infertility remain a challenge in most public health facilities. Moreover, a lack of trained personnel and the necessary equipment and infrastructure, and the currently high costs of medicines are major barriers even for countries that are actively addressing the needs of people with infertility.

A number of different factors may cause infertility, in either the male or female reproductive systems. Female factor for infertility contributes to about 46% of all causes of infertility due to the following:

- Tubal disorders such as blocked fallopian tubes,
- Uterine disorders which could be inflammatory in nature, congenital in nature (such as septate uterus), or benign in nature (such as fibroids);
- Disorders of the ovaries, such as polycystic ovarian syndrome, endometriosis and other follicular disorders;
- Disorders of the endocrine system causing imbalances of reproductive hormones.

Male factors contribute to about 20% of all cases of infertility either due to poor semen quantity or quality. In one third of cases, it's difficult to explain the causes of infertility. About 10% of infertile couples have both male and female contributory factors [(2)].

In general, infertility has emerged as a serious health problem in India. About 8% of infertile couples need serious medical intervention involving the use of advanced Assisted Reproductive Technologies (ART) procedures such as In vitro Fertilisation (IVF) or Intracytoplasmic Sperm Injection (ICSI). Such advanced treatment is expensive and not easily affordable to the majority of Indians. Further, the successful practice of ART requires considerable technical expertise and expensive infrastructure. The likelihood of the success of ART methods depends on different factors. For example, the chance of having an embryo in one IVF cycle depends on the patient's age, the cause of infertility and the history of infertility treatments. IVF is the therapeutic option of reproductive medicine with the highest yield per attempt, coming close on many occasions to that achieved by fertile couples conceiving naturally[(3)].

<u>IVF- An overview</u>

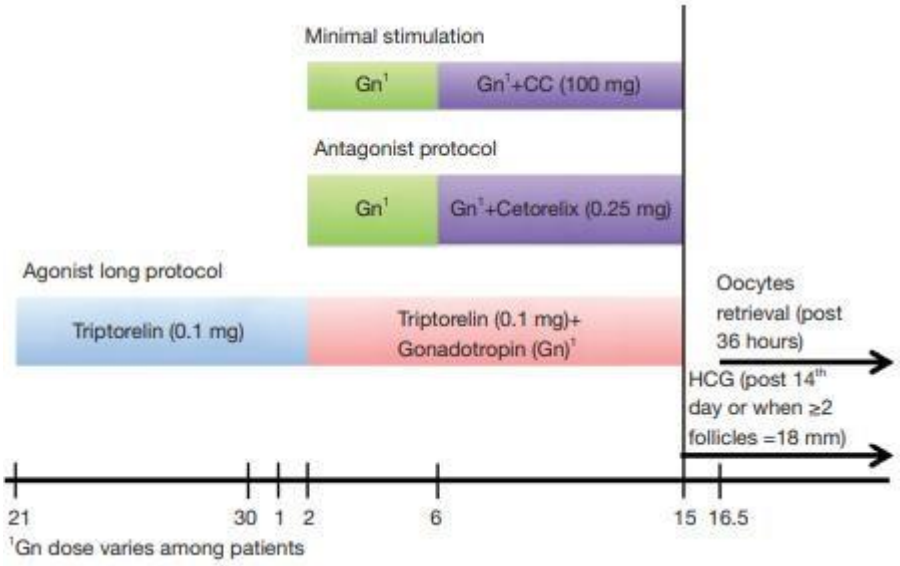
IVF is an assisted reproductive technology where an egg is fused with the sperm outside the body (In Vitro). IVF treatment has 5 basic steps which includes the following:

1. Monitor and stimulate the development of healthy egg(s) in the ovaries.
2. Collect the eggs.
3. Secure the sperm.
4. Combine the eggs and sperm together in the laboratory and provide the appropriate environment for fertilization and early embryo growth.
5. Transfer embryos into the uterus.

These steps are followed by rest. A blood test and potentially an ultrasound will be used to determine if successful implantation and pregnancy has occurred. As with most medical procedures, there are

potential risks related to each step of the procedure.
There are different types of medicines with different mechanisms of action for ovarian stimulation. The choice of the ovarian stimulation protocol depends on various factors like age of the patient, ovarian reserve, risk of complications and past history. Some commonly used stimulation protocols are mentioned in the figure below.

Figure 1: Stimulation procedures for agonist long, antagonist and minimal stimulation protocolsfor IVF.



GN: gonadotropin mixtures; CC: clomiphene citrate

Source: Shrestha D et al.,[(4)]

GnRH (Gonadotropin-Releasing Hormone) antagonist protocols are widely used due to the fear of OHSS, which is comparatively more likely with GnRH agonists and Human Chorionic Gonadotropin (HCG) [(5)]. GnRH analogues are widely used in stimulation protocols either to down regulate the cycle or to prevent the premature LH surge.

Possible complications and management:

Ovary stimulation carries the risk of hyperstimulation, where the ovaries become swollen and painful. This condition, Ovarian Hyperstimulation Syndrome (OHSS), is usually rare and mild. Other side effects of IVF treatment are severe abdominal pain, severe nausea or vomiting, decreased urinary frequency, dark-coloured urine or shortness of breath. Egg retrieval and the use of laparoscopy carry the typical risks associated with receiving anaesthesia. Additionally, there is a slight risk of bleeding, infection, and damage to the bowel, bladder, or blood vessel.

Less than one patient in 1,000 will require surgery to repair damage caused during the egg retrieval process. The chance of a multiple pregnancy is increased in all assisted reproductive procedures. There are additional risks and concerns related to multiple pregnancy including the increased risk of premature delivery.

ART service delivery

Currently, very few public facilities provide ART services. The rising demand is thus met by an

expanding private sector for these services. Although the ART rules regulate these private providers, their prices remain uncontrolled. There is a lack of scientific data to suggest the cost of providing these services in India. This results in huge out-of-pocket expenditure and financial burden on infertile couples. As per a systemic review of financial costs of assisted reproductive technology for patients in low- and middle-income countries, medical costs of one ART cycle are significantly higher (166.4%) than patients' average annual income in India. [(6)]

Regulatory framework for ART services in India currently includes Assisted Reproductive Technology (Regulation) Act, 2021 and ART rules notified under the act. This framework regulates the practice of ART by laying down rules on egg and sperm donation, cryopreservation, registration of ART clinics and sets different criteria for different types of ART clinics[(7)] . Currently, Central Government Health Scheme (CGHS) is reimbursing one time cost of Rs. 65,000 or the actual cost, whichever is lower, incurred for three fresh cycles of IVF as per a government memorandum if the woman/couples fulfil specific criteria.[(8)] With the ART Act, 2021, there is a growing demand to assess if IVF services could be included in the Ayushman Bharat- Pradhan Mantri- Jan Arogya Yojana (AB-PM-JAY) package.

AB-PM-JAY is the largest health assurance scheme in the world which aims at providing a health cover of Rs. 5 lakhs per family per year for secondary and tertiary care hospitalization. Currently, PM-JAY scheme includes medical and hospitalization expenses for almost all secondary care and most tertiary care procedures. However, certain conditions are exempted under this scheme. Fertility treatment being one among them. In view of the rising demand and high financial burden of IVF in India, there was a request from the Health Ministry to Health Technology Assessment in India (HTAIn), Department of Health Research (DHR) to estimate treatment cost of IVF for inclusion in PM-JAY. The HTA Resource Hub at Indian Council of Medical Research- National Institute for Research in Reproductive and Child Health (ICMR- NIRRCH), Mumbai had been allocated this research question. This study was conducted to address this research question.

Note: As per the ART Act 2021, ovum donation is also included in IVF. The expenditure for patients

Chapter 2: Methodology

2.1 Objectives

- To estimate health system cost of diagnosis and treatment of infertility including IVF
- To estimate out-of-pocket expenditure incurred by infertile couples including IVF services
- To assess HRQOL among couples accessing services for diagnosis and treatment of infertility including IVF

2.2 Sampling

Few public health facilities provide IVF services. There are many tertiary healthcare facilities providing IVF services in the private sector. But there was lack of willingness from many health facilities to participate in the study. Two private hospitals agreed to participate, while three hospitals agreed from the public sector. Thus, convenience sampling was used. While selecting the study sites, efforts were also made to spread the sites across different geographical regions of India. The study sites are listed below.

1. Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh
2. Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai
3. Maulana Azad Medical College (MAMC), Delhi
4. SAT Hospital, Government Medical College, Trivandrum
5. Jawaharlal Nehru Medical College (JNMC), Datta Meghe Institute of Medical Sciences, Wardha

Private facilities were included in the study as a large share of service delivery for infertility and IVF comes from the private sector. Thus, it was important to identify the financial burden of these services on patients seeking treatment from private vis a vis public facilities. Moreover, it would also help to identify the infertility management and IVF treatment process as is being practised currently in India.

Sample Size for OOPE:

The sampling method used for OOPE estimation was semi purposive consecutive sampling of patients utilizing the services at selected sites. Using this method of sampling for the data collection period of 6-8 months we could collect data of 150 cases of IVF and 500 cases of infertility diagnosis and management for all sites.

Inclusion criteria

For IVF component, all couples enrolled for IVF in the facility irrespective of diagnosis or outcome and willing to participate in the study were included in the study.

For infertility component, patients who have undergone infertility treatment (including Intra-Uterine Insemination (IUI)) for five selected causes of infertility and willing to participate in the study were included.

Five causes of infertility considered:

1. Polycystic Ovarian Syndrome (PCOS)

2. Endometriosis
3. Tubal factors
4. Uterine factors
5. Male infertility

For costing of IVF and infertility services, relevant cost-centres from these five healthcare facilities were considered.

Exclusion criteria

For the infertility component, patients with idiopathic infertility and multiple factors of infertility were excluded from the study as it is difficult to segregate the expenditure for different factors from patients' perspective.

2.3 Study initiation and management:

- Ethical approval from all the study sites with all translated versions of Participant Information Sheet (PIS) and consent forms was obtained before study initiation.
- One Senior Research Fellow and one Medical Social Worker were recruited for data collection at each study site. Virtual training sessions were held where the data collectors were trained by principal and site investigators. They were also trained in soft skills to be sensitive to the stress and psychological stigma of the patients undergoing infertility and IVF treatment.
- All the data collection tools, along with participant information sheets and consent forms, were printed and sent to the study sites.
- In-person monitoring visits were conducted at study sites to guide the data collectors and solve the ground challenges faced in data collection.
- For health system costing data collection, necessary approvals were taken as per the institutional requirement. These approvals were facilitated by site investigators and collaborators.
- The collected data was entered simultaneously at NIRRCH and the quality of data was monitored.
- Weekly discussion meetings were arranged with the data collectors from all the sites to monitor the progress and solve the queries related to data collection.
- At the end of data collection, all the signed consent forms and data collection tools were sent back through courier from the five sites. They are stored at ICMR-NIRRCH.
- During data analysis, virtual meetings were held with all the investigators and collaborators to discuss the interim results and get their inputs in data analysis.

2.4 Data collection

OOPE was categorized into three distinct cost components for better clarity on the financial burden.

1. Direct Health Costs: This category encompasses the most readily apparent expenses, including registration fees, consultations with specialists, diagnostic tests, and the actual treatment procedures themselves.
2. Non-Medical Costs: These often-overlooked expenses include travel costs associated with treatment, such as transportation and accommodation, as well as food expenses incurred during treatment cycles.
3. Indirect Costs: This category captures the hidden financial impact of infertility treatment. It considers lost wages due to missed work for both the patient and any accompanying person during the treatment process.

For data collection on OOPE, tools were designed to capture the data from patients' perspective. The tools were designed following consultations with IVF experts and literature review. The same were finalised after pilot testing and translated to local languages. For OOPE, standard tool was modified to ensure all expenditure at various stages of seeking care for infertility including IVF was captured. The details on the expenditure obtained from the patients interviews were validated with the actual their bills of expenditure.

For HRQoL, the tools were procured from EuroQol separately for each language that sites demanded. Two tools were used for data collection of HRQoL of the participants- 1. Five-dimensional Euro-QoL questionnaire (EQ-5D-5L) and 2. Visual Analogue Scale (VAS). These tools were administered to collect self-reported data of HRQoL when the patient had come for follow-up visit either for diagnosis or scheduled treatment visit. EQ-5D questionnaire includes five dimensions describing health states - Mobility, Usual Activities, Self-Care, Pain & Discomfort, and Anxiety & Depression and five levels of the problem along with a number string representing no=1, slight=2, moderate=3, severe=4 & unable to=5 in each of these five health states. Couples were asked to tick boxes to indicate the level of problem they experienced on each of the five dimensions along with the reason for the response. In the Virtual Analogue Scale (VAS), couples were asked to mark their current health status on the VAS ranging from 0 (worst imaginable health) to 100 (best imaginable health) to capture the overall assessment of health. The EQ VAS therefore provides information that is complementary to the EQ-5D profile.

For IVF, the patients undergoing IVF, preferably at the stage of embryo transfer and fulfilling the inclusion criteria were enrolled. They were followed retrospectively to capture the costs incurred only for IVF upto last three cycles. The limit of three cycles was in line with the expert opinion suggesting the optimal number of IVF cycles to be three, beyond which the risks outweigh the potential of pregnancy.

For infertility, the patients undergoing infertility diagnosis and treatment upto IUI other than IVF fulfilling the inclusion criteria were enrolled and expenditure incurred in last one year was obtained.

For OOPE and HRQoL of IVF and infertility participants, data was collected by personal interviews of participants when the patients visited the facility for diagnosis or treatment. Whenever the participants were unsure about their expenditure amount, the bills available with them were used to ascertain the expenditure data. While collecting the data on HRQoL, the participants were probed to identify their quality-of-life score keeping in mind the whole IVF cycle or infertility management as applicable.

For health system costing, the health system perspective was considered to estimate the cost incurred by the government for providing IVF services[11]. A pre-tested pre-validated costing tool was used for data collection. The cost-centres for IVF and infertility management were identified by expert consultation, observation and literature review. After taking necessary approvals, the data was collected through personal interviews, administrative records and direct observation from relevant cost-centres. Economic costs of resources were considered for data collection. i.e. the cost of donated items was also recorded. The data of one year time period was collected starting from April 1, 2022 to March 31, 2023.

The collected data of OOPE and HRQoL was entered in IBM SPSS version 20. The health system cost data was entered in MS Excel.

2.5 Data analysis

The entered data was cleaned and analysed using IBM SPSS version 20 and MS Excel software. During cleaning of data, expenditure data from cross-sectoral treatments was identified and excluded from the analysis i.e. private sector patients with treatment from public health facilities and public sector patients with treatment from private sector. For example, among participants of three public health facilities, many cases were identified where patients had undergone previous IUI or IVF cycles in the private sector. Such data was excluded from the analysis as they would give falsely inflated figures of OOPE incurred by patients undergoing treatment in public health facilities. Nevertheless, the expenditure incurred in the private sector while undergoing treatment at public health facilities was included in the analysis as it indicates the challenges with utilisations of public health services. For example, at public health facilities, many patients went to the private sector for lab investigations even after the services were available in the public health facility. This resulted in the out-of-pocket expenditure of patients taking treatment from the public sector. Thus, OOPE results in public health facilities should be seen in light of the available knowledge on challenges in accessibility and utilisation of public health services.

HRQoL:

The EQ-5D-5L Indian value tariff set was used for calculating the utility score of the participant. The combination of each response under each dimension describes that person's EQ-5D self-reported health state, often called an EQ-5D profile.

Out-of-Pocket Expenditure-IVF:

Out-of-pocket expenditure was collected using the adapted OOPE tool consisting of Direct Health Costs, Non-medical costs, and Indirect Costs incurred by the couple during one IVF cycle. OOPE was collected at each stage of the IVF cycle from the Pre-IVF cycle, Follicle Study, Oocyte retrieval/Ovum Pickup (OPU) to Embryo Transfer (ET) (Fresh or Frozen).

The collected data was analysed to assess direct health costs, non-medical costs and indirect costs. The charges paid for registration, consultations, USG, blood tests and medicines were considered as direct health costs. In addition to this, diagnostic procedure cost along with any laparoscopic procedure cost in the Pre-IVF stage, oocytes retrieval and embryo transfer (Fresh or Frozen) cost for procedure, hospital admission costs, semen donation, semen donor charges (if applicable), cryopreservation charges (if applicable), hospital admission charges with drugs cost in case of OHSS or any other complications were considered under direct health cost. The share of these components in total direct health cost was also analysed

Under non-medical costs, total travel costs, total food costs, and total lodging costs for all the visits during all four stages of the IVF cycle were considered including that of the bystander. The share of different components in the total non-medical cost was also analysed.

Under Indirect costs, total loss of wage due to work missed for the husband, wife, and any other accompanying person was analysed.

Note: *As per the comments received from TAC cost of ovum donation was identified from the study site. The cost for ovum donation as per the ART Act 2021 includes expenditure in terms of oocyte donor charges, medicine cost and insurance. The expenditure on medicine is similar to any other female receiving IVF treatment and is already captured in the package cost. The only additional expenditure in case of ovum donation will be oocyte donor charges and insurance coverage which will*

be part of OOPE.

Out-of-Pocket Expenditure-Infertility:

The tool had captured expenditure of infertility patients in last one year. Direct health costs in these patients included costs of registration, consultations, investigations, medicines, diagnostic and therapeutic procedures, and admission charges (if any). It also included direct health costs incurred due to complications following infertility treatment. The share of these components in total direct health cost was also analysed.

Non-medical costs covered the total travel costs, total food costs, and total lodging costs for all the visits during past one year for infertility management including that of the bystander. The share of different components in the total non-medical costs was also analysed.

Indirect costs included total loss of wage reported by participants due to work missed for the husband, wife, and any other accompanying person.

The direct health costs, non-medical costs and indirect costs incurred during 1 IUI were also analysed.

Out-of-pocket expense varies as per diagnosis of infertility as well as at which hospital the services are availed. The current data for OOPE has been very heterogeneous and skewed. Hence mean values for several cost parameters couldn't be derived. Median values with Inter quartile range (IQR) 25^{th} and 75^{th} percentile is presented.

The study went a step further by comparing OOPE across public and private healthcare sectors and factor wise analysis to identify the financial burden in case of single factor infertility due to each of the five selected factors. The five factors taken into consideration were endometriosis, male infertility, PCOS, tubal factor and uterine factor. This analysis helps to identify potential disparities in the financial burden faced by patients depending on where they receive treatment.

Financial burden of IVF and rest of the infertility treatment was estimated from two data points. As part of the annual household consumption expenditure data, patients had given the amount spent by them for infertility treatment (including IVF) in the past year. From the collected data on treatment expenditure, we have analysed the total OOPE of the patients for one IVF cycle and for one year of infertility treatment. These estimates suggest the financial burden of ART on patients in India. For both IVF and infertility participants, burden of catastrophic health expenditure was also analysed. The threshold for catastrophic health expenditure was taken as 10% of annual household consumption expenditure as recommended by the WHO [(12)].

Health system costing- IVF:

A mixed method micro-costing was done using primary data from a health system perspective. Major cost-centres of IVF services included Out Patient Department (OPD), Laboratory, Sonography room, IVF Operation Theatre (IVF-OT) and wards. The adjoining small cost-centres were grouped under these major centres for analysis. The OPD included the cost-centres of registration room, consultation room, reception area, waiting area, examination room, store room, record room, washrooms and OPD corridors. The cost-centres of semen collection room, semen processing lab and embryo/IVF lab were grouped under the larger category of Laboratory. The cost-centres of scrub room, changing room, pre and post-operative care room, OT, OT corridor, nurse room, and washroom were the usual cost-centres

grouped under the larger category of OT-IVF.

Cost of resources were divided into fixed and variable costs. Fixed costs included the costs that were incurred irrespective of the volume of service users. While variable costs changed with the volume of service delivery i.e. number of IVF cycles conducted in the year. Classification of costs in these two categories is given in the table below.

Table 1: Classification of fixed and variable costs in health system costing

Fixed costs	Variable costs
· Costs of infrastructure/rental · Furniture and fixture cost · Costs of equipment including their maintenance · Fixed monthly salary of human resources · Overheads like electricity, water, phone, internet charges	· Case based HR payments · Costs of consumables and stationery · Medicine costs

Apportioning: Cost of all the components for any cost-centre was apportioned for IVF patients using different apportioning factors as mentioned in the table below.

Table 2: Apportioning factors for cost-components

Cost component	Apportioning factor
Infrastructure (Building rental cost, electricity, water, phone, tax)	Area of the cost-centre
Furniture & Fixtures	Number of patients
Non-medical equipments	Number of patients
Consumables, stationary	Number of patients
Medical equipments	Number of patients (ETs done)
HR	Time allocated, number of patients
Medicines	Mean frequency, procurement price (if available) or IndiaMart price
Lab tests	Mean frequency, unit costs (From CHSI)
IPD	Number of bed-days

The number of ETs were taken as the number of IVF cycles in the reference year. Not all OPUs lead to ET and complete IVF cycle. Some IVF patients must have not reached till ET, while some patients would have had multiple ETs after OPU. For uniformity of calculation across all sites, we assume that they will average out and every ET is following the previous processes of IVF cycle.

Every site had some differences in their IVF service delivery, which were accounted for at all sites. Detailed methodology used for costing of different cost-components and cost-centres is described below.

Human resources (HR):

The cost of human resources had both fixed and variable cost components. At most sites, human resources had fixed hours of service delivery for OPD and USG room. Also, at most sites there were no separate hours of service delivery for IVF patients. For these cost-centres, top-down approach was used where total remuneration of different human resources delivering IVF services was apportioned using time allocated for service and number of patients as apportioning factors to derive the cost of per service delivery.

E.g. Cost of HR for one OPD consultation= Total remuneration per working hour of HR A,B,C,..* total hours of OPD service delivery in the year/ total OPD consultations in the year

For the cost-centres of OT, Lab and ward, the hours spent on the service delivery were not fixed. Thus, a bottom-up costing approach was used for HR in these cost-centres.

E.g. Cost of HR for one ovum pick-up (OPU)= Total remuneration per working hour of HR A,B,C,…. * total time contributed for one OPU by HR A,B,C,…

The costs of HR called on per-case basis was added to relevant cost-centres. E.g. The anaesthetist at all sites was called on per case basis at fixed remuneration per case of OPU, which was added in the cost of HR for OT.

<u>Fixed costs</u>

Infrastructure:

This cost-component includes the cost of building construction/ rental and overheads like property tax, building maintenance cost, phone, internet, electricity and water charges. All the study sites had their own building and didn't pay any rent. Monthly rental price of 100 square feet in the locality was collected from online sources or personal interviews of people residing in nearby areas. The annual rental cost for the area of different cost-centres was derived from this data and was used as a proxy for rental cost. Annual expenditure on different overheads mentioned above was captured from the hospital records. These expenditures were allocated to different cost-centres using area as the apportioning factor. This apportioned cost was then allocated to service users to derive the unit costs E.g. infrastructure cost per OPD visit.

Furniture and fixtures

The number of furniture and fixture items in each identified cost-centre was captured through observation. Their cost was captured from the administration department. Thus, total cost of furniture and fixtures for each cost-centre was derived. Its Equivalent Annual Cost was derived with 3% discount

rate and 10 years of expected use.

Equipments: Medical & non- medical

The total price of the equipment and its expected life were collected from hospital records. Based on this data Equivalent Annual Cost of the equipment were derived at 3% discount rate. The uses of the equipment were identified to derive the number of total users. Using this denominator, Equivalent Annual Cost per unit of use was derived.

Variable costs

Consumables and Stationery

The annual expenditure on consumables and stationery was collected from administrative records. From the total cost of these items for a cost-centre, cost per unit of service use was derived.

Medicines

Majority of the medicines prescribed during IVF were not available in the public system. Thus, even at public facilities, patients were purchasing these medicines from the market by paying out of their pockets. The burden of this expenditure is reflected in OOPE of IVF patients. Very few of the commonly prescribed medicines for IVF patients were available in the public system. Their procurement price list was available only at the Delhi site. These prices were taken as a proxy for all sites. While deriving the cost of IVF in the current setting, the cost of medicines not available in the public system was excluded. It is important to estimate the IVF cost if these medicines were to be provided from public facilities and also for the purpose of reimbursement. To estimate this, lowest IndiaMart prices of medicines were considered. But given the bargaining power of the government, the public procurement prices might be even lower than this assumed cost. Deterministic sensitivity analysis at 20% variation was conducted on these prices. This analysis gives the cost of one IVF cycle along with medicines.

Cost from different cost-centres

Total cost of all the cost-components of OPD was then used to derive the cost of 1 OPD consultation. For this, total OPD consultations conducted in the reference year was used as the denominator. This unit cost was multiplied with the number of OPD visits required for 1 IVF cycle. This frequency was derived from the study data of 148 couples. Using the same methodology the cost for radiography and ward-days were derived for 1 IVF cycle.

From the total fixed costs of infrastructure, furniture and equipments, cost of 1 operational hour was derived using the following formula. Based on the expert consultation and observation, IVF OT is occupied for a total of four hours for one patient, which includes the time taken for the procedures of ovum pick-up, embryo transfer and sterilisation.

For cost-centres of IVF OT and IVF Lab, the fixed cost was dependent on the number of IVF cycles performed at the facility. To resolve this, expert consultations were held and based on those discussions, the approach of analysis was changed for these cost-centres to separate the cost from the number of IVF patients catered. Per hour cost of running IVF OT and IVF lab was derived by dividing the total fixed cost of these cost-centres (infrastructure, medical equipment, furniture and fixtures) with the number of hours for which OT or Lab is operational. This per hour cost was then multiplied with four i.e. the number of hours for which OT is utilised for one IVF patient. For human resource cost at IVF OT and

IVF lab, bottom-up costing was used where time of each category of HR for one IVF cycle was multiplied by their salary per working hour. The variable cost per patient does not change with total IVF patients in the facility. Thus, variable cost for IVF OT and IVF lab was derived using the same methodology as rest of the cost-centres (OPD, USG room, etc.). In this, the total cost incurred was divided with the number of IVF patients catered to by the facility to derive the cost of one IVF patient.

In case of wards, only the facility at Trivandrum site had separate ward for IVF and infertility patients. Thus, their cost data was used as a proxy for costing of two bed-days at other sites. There was variation in the practices of inpatient days for one IVF cycle. For example, the Chandigarh site had no IPD days for IVF cycle. But since the majority of sites had total two IPD days per cycle, the cost of two bed-days was added in the IVF costing across all sites.

The expenditure data of kitchen and laundry was available only at the Chandigarh site, which was used to derive the total kitchen and laundry cost for one IVF cycle and was used as a proxy for other sites as well. The costs of common lab tests were taken from the Costing of Health Service in India (CHSI) data.

Based on this analysis, the cost-function for one IVF cycle is mentioned here.

Total cost of 1 IVF cycle = Unit cost of OPD visit *6+ OT and IVF lab costs for 1 IVF patient + unit cost of USG *8 + cost of 2 bed-days + cost of common lab tests+ cost of medicines + cost of kitchen & laundry

Health system costing-Infertility:

The management of infertility, as is currently practised, was captured in the 500 participants of the study. From this data, the frequency of different diagnostic and treatment interventions for management of five factors of infertility for one year was derived. Based on this, cost functions were derived for health system costing of infertility services.

Total cost of managing single factor infertility due to X for 1 year= frequency of diagnostic test A,B,C * unit cost of diagnostic test A,B,C……+ frequency of any other diagnostic intervention * unit cost of any other diagnostic intervention + frequency of OPD visit* unit cost of OPD visit + cost of IPD bed-days (if applicable) + cost of surgery (if applicable)

The major cost-centres for infertility management were identified and their total cost of resources for a span of one year was captured. These cost-centres were OPD, OT, Lab, IPD, kitchen and laundry. Majority of these cost-centres were common with IVF services. Cost of one outpatient consultation and one ultrasonography was derived using the methodology as discussed in the IVF results section. Cost of diagnostic laboratory tests and surgical procedures were taken from the CHSI study. The proportion of patients undergoing surgical treatment as part of infertility management was very less. The cost of common surgical procedures along with their IPD costs is discussed below. The usual hormone medicines prescribed as a part of infertility management were not available in any public system. Thus, most of the medicines were purchased by patients from the market by spending out of their pockets. The burden of this is captured in the findings of OOP expenditure for medicines discussed later in this report. The health system cost of infertility management excludes the cost of medicines.

Chapter 3: Results

3.1 Analysis of costs and quality of life among cases undergoing InVitro Fertilisation

The sample for this component included couples who were undergoing IVF treatment. Thus, only the expenditure incurred by them once they started the IVF cycle till the embryo transfer was captured and analysed. This also included any expenditure on complications in the course of IVF. At all sites where ICSI was performed in the study period, there was no difference in the amount charged from patients as procedure charges. During the study period, the share of ICSI in the total annual IVF cycles was 0% at PGIMER, Chandigarh; 90% at JNMC, Wardha; 64% at SRIHER, Chennai; 88% at SAT, Kerala and 0% at MAMC, Delhi.

3.1.1 Patient profile-IVF:

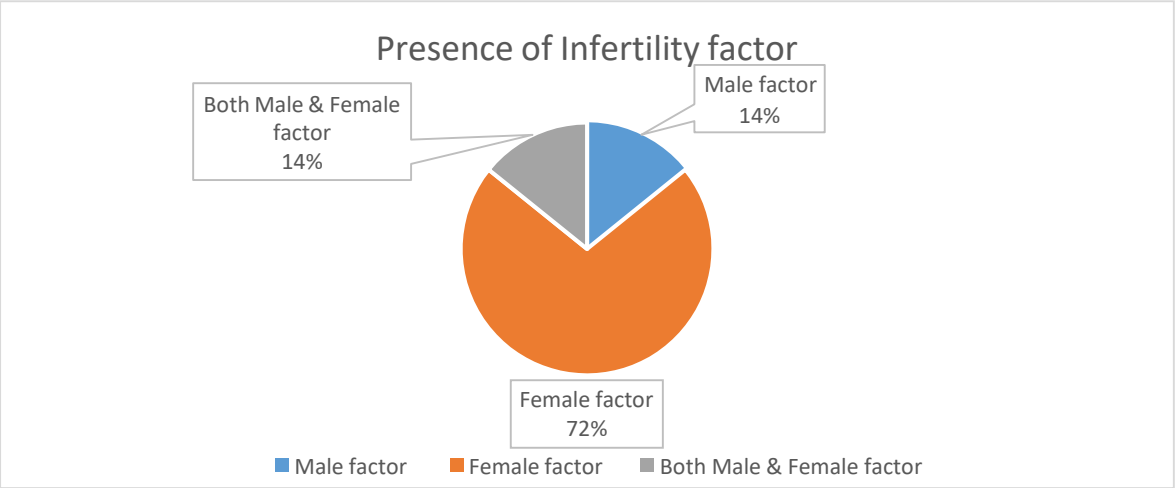
Out of the proposed 150 couples, total 148 couples undergoing IVF were enrolled across 5 study sites. This shortfall was due to low IVF patient load at one study site (PGIMER, Chandigarh) during the study period. The demographic profile of the participants is depicted in the table below.

Table 3: Background characteristics (IVF)

N= 148	Male	Female
Age in years (Mean±SD)	37 (±5)	33 (± 5)
Education	Illiterate-0% Primary-6.8% Secondary-17.6% Higher Secondary - 17.6% Diploma-5.4% Graduate-37.8% Post graduate-14.2% PhD-0.7%	Illiterate-0% Priamry-5.4% Secondary-13.5% Higher Secondary-16.2% Diploma-2% Graduate-39.2% Post graduate-22.3% PhD-1.4%
Employment	100%	21%
Married since (Mean±SD) years	8 (±4)	
Years of undergoing infertility treatment (mean ±SD)	6 (±4)	
Number of clinics visited for the treatment (mean ±SD)	4 (±3)	
Type of infertility	Primary: 59% Secondary:41%	
Family history of infertility	Male- 7% Female-6%	
Tobacco consumption	Male-18% Female-1%	
Alcohol consumption	Male- 19% Female-2%	
Underwent IUI No. of IUI cycles(Mean ± SD) Donor sperm used in the current cycle	49% 3 (±2) 6%	
Annual household income (Median, IQR)	Rs. 3,60,000 (240000,600000)	
Co-morbid conditions History of hypothyroidism: History of Diabetes: History of previous surgeries:	 Male: 0% Male: 13% Male: 0%	 Female- 30% Female-0% Female-58%

Couples reported that on an average they were spending 29% (± 15%) of their total household consumption expenditure on infertility treatment including IVF. The causes of infertility among enrolled participants is depicted below.

Figure 2: Causes of infertility in IVF participants



Majority (72%) of the participants undergoing IVF had female factor infertility. Causes of male and female factor infertility amongst the participants are mentioned in the pie chart below.

Figure 3: Causes of infertility- Male (IVF)

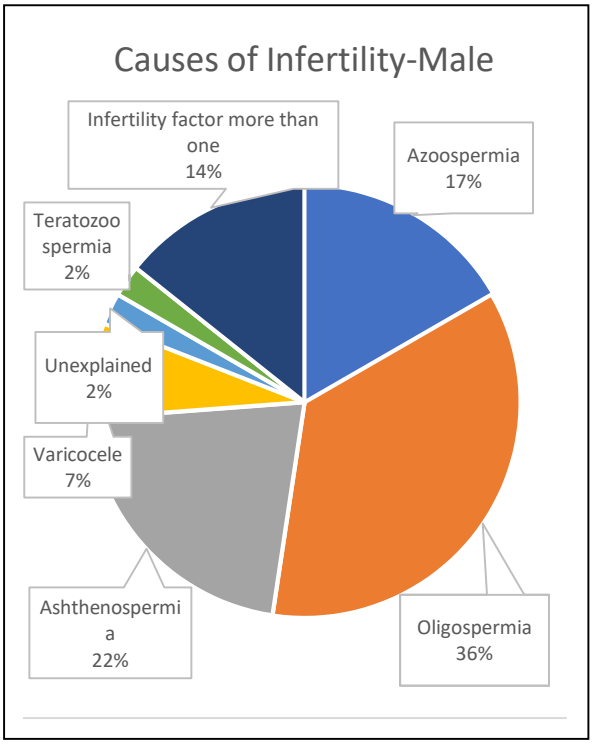
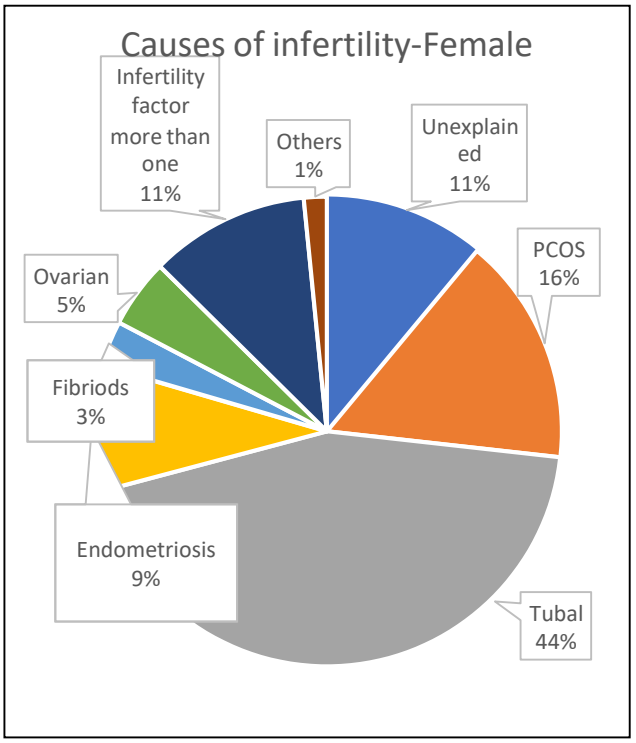


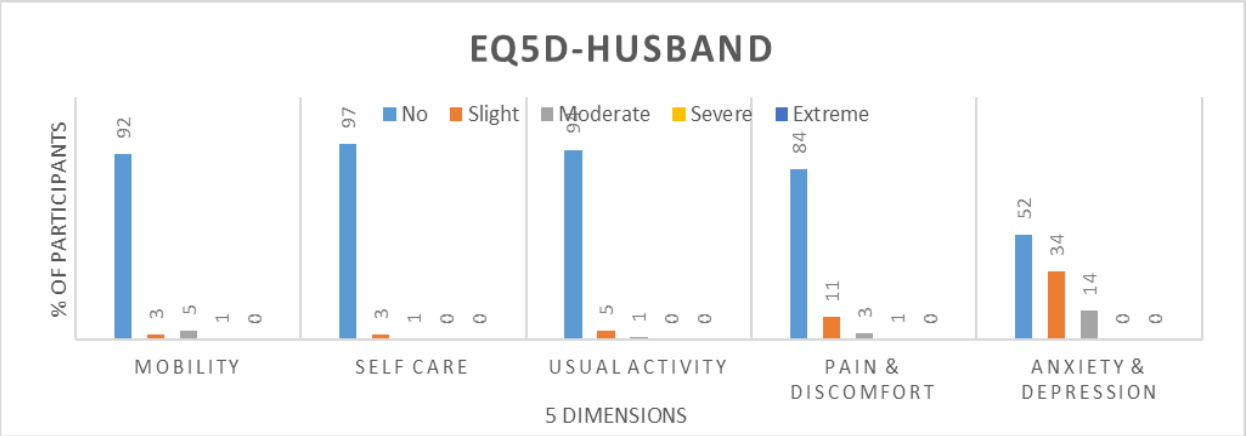
Figure 4: Causes of infertility-Female (IVF)



Oligospermia and tubal factor infertility were the leading cause of infertility among male and female participants undergoing IVF.

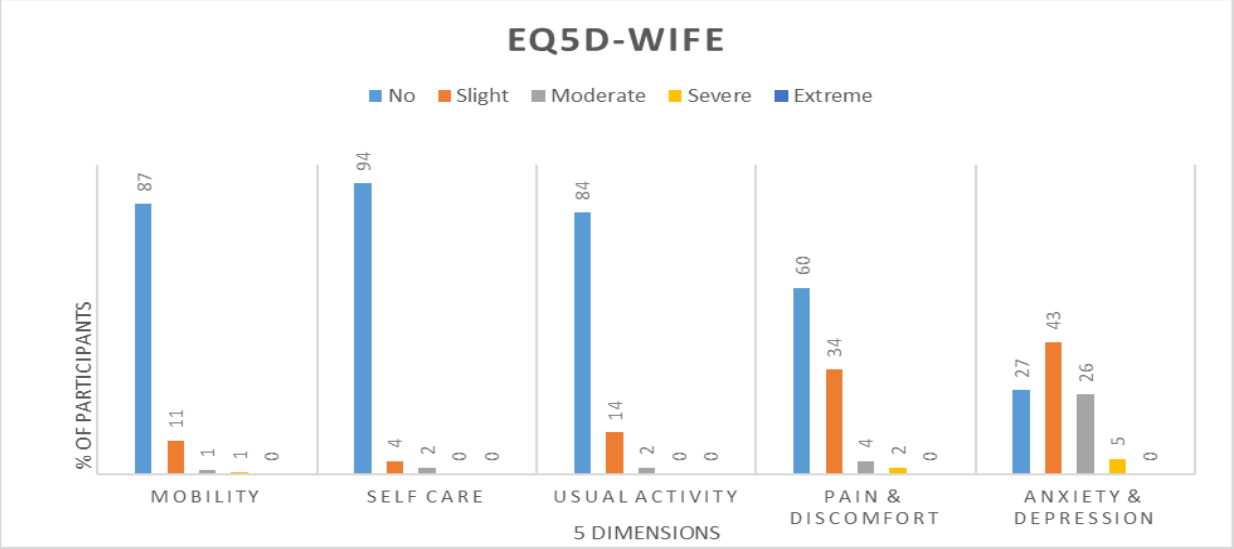
3.1.2 Health-Related Quality of Life of IVF couples

Figure 5: EQ5D-Husband



As is evident from the graph, among the five dimensions of quality of life, mobility, self-care and usual activities were not affected in males. Among male participants, the share of those reporting slight and moderate anxiety & depression was 35% and 15% respectively due to infertility issues. More than 90% of them have reported having no problems regarding self-care and usual activity and no other extreme dimension was noted; however, 11% reported slight pain and discomfort due to other health conditions like back pain.

Figure 6: EQ5D-Wife



Amongst the five dimensions, 74% of wives reported feeling slight to severe levels of anxiety and depression due to being unable to conceive. 40% reported having slight to severe forms of pain and discomfort after ovum pickup, during different stages of the IVF procedure, and due to other

conditions like back pain. While the majority of them had, no problems related to mobility, self-care, and usual activities; however, some of them reported having slight problems.

The mean utility score for the husbands was 0.95 (±0.07) and 0.918 (±0.12) for wives. The average VAS scores for the husbands and wives were 84.45 (± 13.47) and 78.68 (±16.66) respectively.

3.1.3 Out-of-pocket Expenditure incurred by couples undergoing IVF:

Table 4: Out-of-pocket Expenditure- IVF

Study sites	Fixed hospital charges (Fixed Direct Health Cost)				Expenditure incurred additional to the hospital package (Average) *only those participants who had incurred indirect cost was considered			Total expenditure of patient Mean±SD
	1 OPU + 1 ET procedure charges	Medicines as part of initial payments	Other payments to hospital	Average cost paid as fixed hospital charges	Direct Health Cost (Investigations, procedures & drugs) Mean±SD	Non Medical (Food, travel & lodging) Mean±SD	Indirect health cost (Loss of wage- Husband & wife) Mean± SD	
PGIMER, Chandigarh (Public)	Rs. 23,000	-	Rs.15,000 for embryo freezing (If applicable)	Rs.23,000	Rs. 55,529 (±18,450) Includes freezing charges	Rs.11,055 (± 10,212)	Rs.3614* (± 1,787)	Rs.90,616 (± 22,485)
MAMC, Delhi (Public)		-	1700 for leaf (Max 3 embryos/leaf) (if applicable)		Rs.45,479 (± 16,093)	Rs.5778 (±2,516)	Rs.3618 (± 3,174)	Rs. 54,876 (± 21,782)
SAT, Trivandrum (Public)	Rs. 25,000	-	Rs. 15,000 for disposables	Rs. 40,000	Rs. 1,13,067 (± 83784)	Rs. 18802 (± 13619)	Rs.11,653 (± 10,465)	Rs. 1,83,522 (± 84,952)
AVBRH, Wardha (Private)	Rs. 38,602	Drugs Rs. 40,000	Rs. 3898 for investigations, Rs. 4000 for bed charges, Rs. 4000 for consultancy	Rs. 95,000	Rs. 33,020 (± 25,153)	Rs.3507 (± 3305)	Rs.4050* (± 3,025)	Rs. 1,32,337 (± 26,932)
SRIHER, Chennai (Private)	1 OPU + 1 ET + 1 ICSI= Rs1,14,000	Rs. 80,000	Rs. 3,450 (for registration + cryopreservation)	Rs.1,97,450	Rs. 100017 (± 58718) + Rs. 15863 (± 4209) (Miscellaneous/overhead)	Rs.11,806 (± 6981)	Rs.6104* (± 5,075)	Rs. 3,29,000 (± 60,734)

The total average expenditure of the participants was highest at SRIHER hospital Chennai and lowest at MAMC, Delhi. Amongst the public and private hospitals, highest total average expenditure was

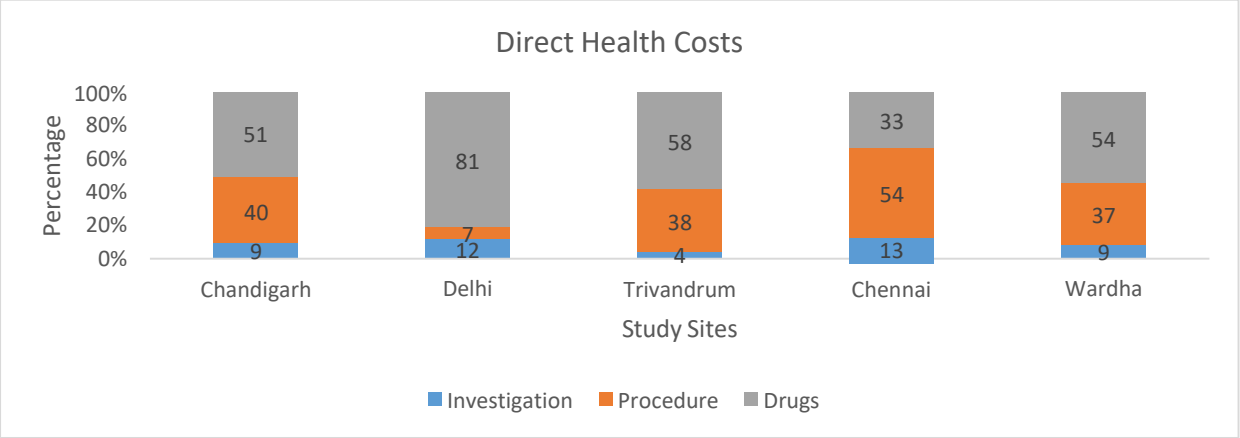
reported at SAT, Trivandrum and SRIHER, Chennai respectively; with lowest at MAMC, Delhi and JNMC, Wardha respectively. It was observed that in every hospital, couples availing IVF had to pay a fixed amount at the time of registration. Over and above this amount, all participants incurred additional expenses. Details are mentioned in table above.

The share of OOPE on 1 IVF cycle in the total annual household consumption was 31% (± 26%) among the participants. Majority ie 88.5% couples were spending more than 10% of their total annual household consumption expenditure as OOPE for one IVF cycle which amounts to catastrophic expenditure.

Around 5% of the participants had insurance coverage for IVF treatment. The median annual insurance instalment was Rs.6000 (IQR-0, 17750) and an average of Rs. 1,00,625 (±35,500) of the treatment expense was covered by insurance. Majority of the participants (58 %) had obtained financial support of which 60% had borrowed from friends and family while others had taken bank loans or gold pledges.

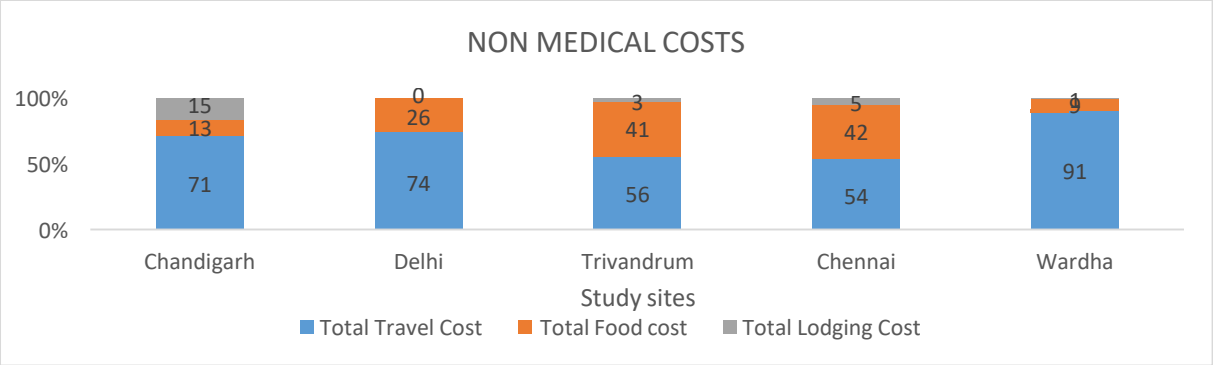
The share of different components in the total direct health costs, non-medical costs and indirect costs is depicted in the charts below.

Figure 7: Direct Health Costs (IVF)



Participants from MAMC, Delhi reported spending around 81% of the total direct health cost expenditure on drugs and the less on investigations and procedures as being a public hospital, investigations are free of cost and even though some medicines were available in the system, no hormonal injections and drugs for IVF were available causing OOPE. Although the participants at Trivandrum procured drugs at a subsidized rate; more than 50% of the direct health costs were incurred on drugs. At Chennai, comparatively many participants had undergone hysterolaproscopy, sonosalpingography, and cryopreservation and the charges for these procedures also was relatively higher than other sites thus raising the overall procedure cost.

Figure 8: Non-Medical Costs (IVF)

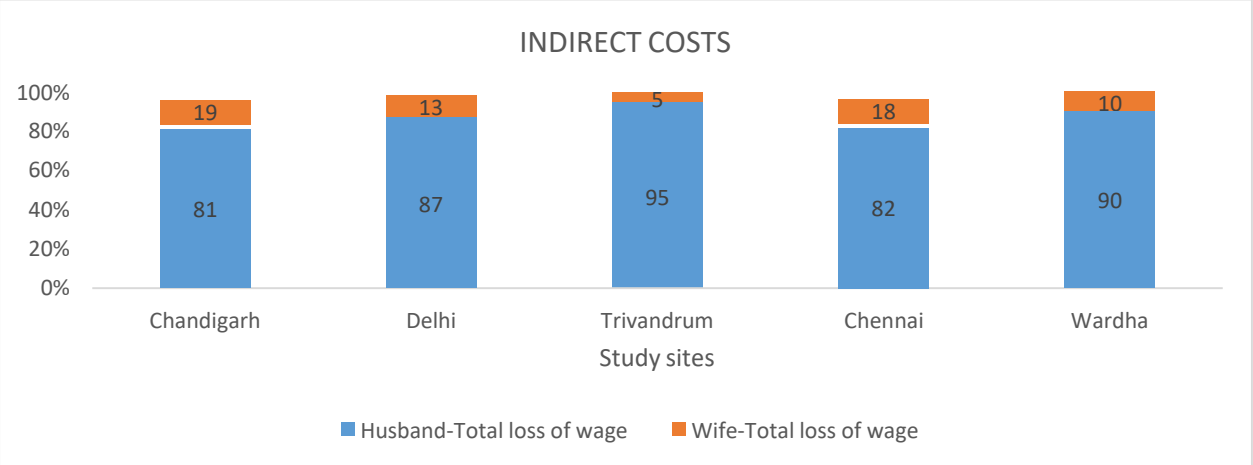


Participants from Wardha, Delhi & Chandigarh reported spending the highest on travel as the median distance travelled from residence to hospital was more leading to greater travel costs at these sites. More than 40% of the expenditure on non-medical costs was due to expenditure on food by the participants visiting Trivandrum and Chennai study sites. Lodging cost was highest at Chandigarh as a greater number of the participants were from neighbouring states and they stayed there through the IVF process.

Table 5: Distance from residence travelled by patients (IVF)

Study sites	Distance travelled in kms	
	Median	IQR (25^{th},75^{th})
Chennai	21.5	4,14.25
Trivandrum	43.9	20.5,57.5
Delhi	43.7	8.85,20
Chandigarh	75.6	31,96.25
Wardha	119.7	16,192.5

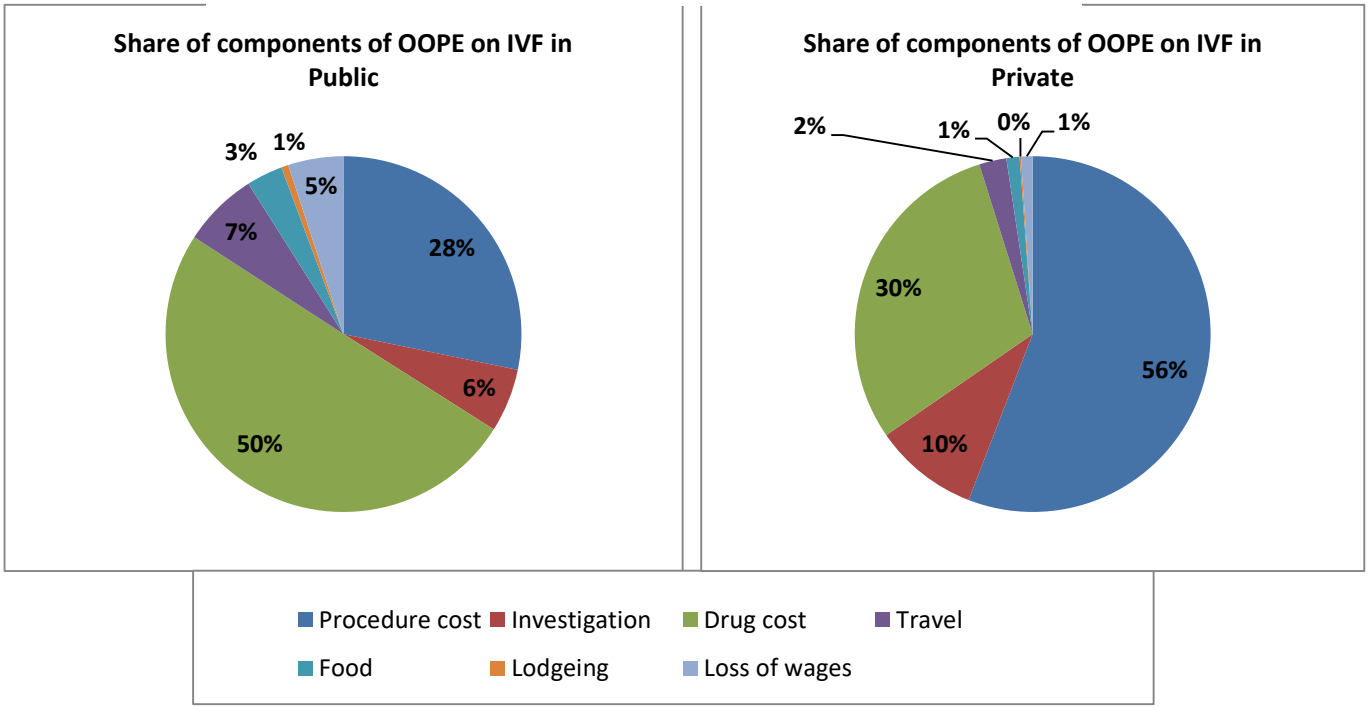
Figure 9-Indirect Costs (IVF)



In indirect costs, loss of wage due to missed work of the male participants accounted for more than 80% of expenditure across all sites. Loss of wage of female participants was highest at PGIMER and SRIHER, Chennai followed by MAMC, as more females from these sites were employed leading to missed work and loss of wage.

Share of components of OOPE on IVF based on type of facility:

Figure 10: Share of components of OOPE on IVF



The overall average OOPE for IVF was Rs. 1,61,893 (±1,08,254). Those who availed the service in public facility for them the average OOPE was Rs. 1,10,104 (±75,503) and for those at private facility the average OOPE was Rs. 2,37,851 (±1,09,556). In terms of various components of OOPE, at public facilities the expenditure is highest for drugs followed by procedure cost and investigation. At private facilities the expenditure is highest for procedure cost, followed by drugs and investigation.

3.1.4 Health system costing of IVF:

Initially, the costing analysis was done using the current utilisation frequencies. As there is huge variation in the utilisation of IVF services across sites, this analysis led to a wide range of cost for one IVF cycle. This analysis was dependent on the number of IVF users at the health facility. The mean cost of providing one IVF cycle at current utilisation frequency is Rs. 1,24,682 (+/- 99,308) without medicines. The range of this cost is between Rs. 48,688 and Rs. 2,89,577. The wide range in the cost was mainly because of the difference in the number of total IVF cycles at different sites.

To estimate the cost of IVF cycle with medicines, we considered the lowest price of those medicines on India Mart to estimate the health system cost of IVF if those medicines were provided from the public sector. Considering the bargaining power of the state, the cost of medicines can be even lower than this. With our assumption, the cost of medicines for one IVF cycle is Rs. 27,100 (21,680- 32,520). Adding this in the health system cost of one IVF cycle, the amount will be Rs. 1,51,782 (+/- 99,308). The derived cost of one IVF cycle at each site is depicted in the table below.

Table 6: Health system cost of IVF cycle at current utilization

Site name	Number of IVF cycles in the reference year	Cost of 1 IVF cycle (without medicines)
PGIMER, Chandigarh	22	Rs. 2,89,577
SAT, Trivandrum	199	Rs. 80,159
MAMC, Delhi	132	Rs. 1,44,421
SRM, Chennai	153	Rs. 60,566
AVBRH, Wardha	182	Rs. 48,688

As the denominator (the number of IVF cycles) reduced, the cost per cycle was proportionally higher. Thus, in this analysis, the cost of IVF was dependent on the operational efficiency of the facility which itself is a dynamic parameter. Such an analysis also reduces the accuracy of the final costing result.

In view of this, the cost of running the OT and lab for one hour was calculated assuming that it would be functional for eight hours per day excluding holidays. It was learnt that one IVF cycle would consume four hours of OT and lab. This per hour cost was then multiplied with four i.e. the number of hours for which OT is utilised for one IVF patient. This per IVF cycle cost for OT and Lab was considered in the formula mentioned earlier while all other costs were based on service utilisation numbers. With this approach, the mean cost of one IVF cycle without medicines was Rs. 54,232 (+/- 12,849) with the range of Rs. 41,001 and Rs. 72,091. The mean cost of one IVF cycle along with medicines was Rs. 81,332 (+/- 12,849). The derived cost for each site is depicted in the table below.

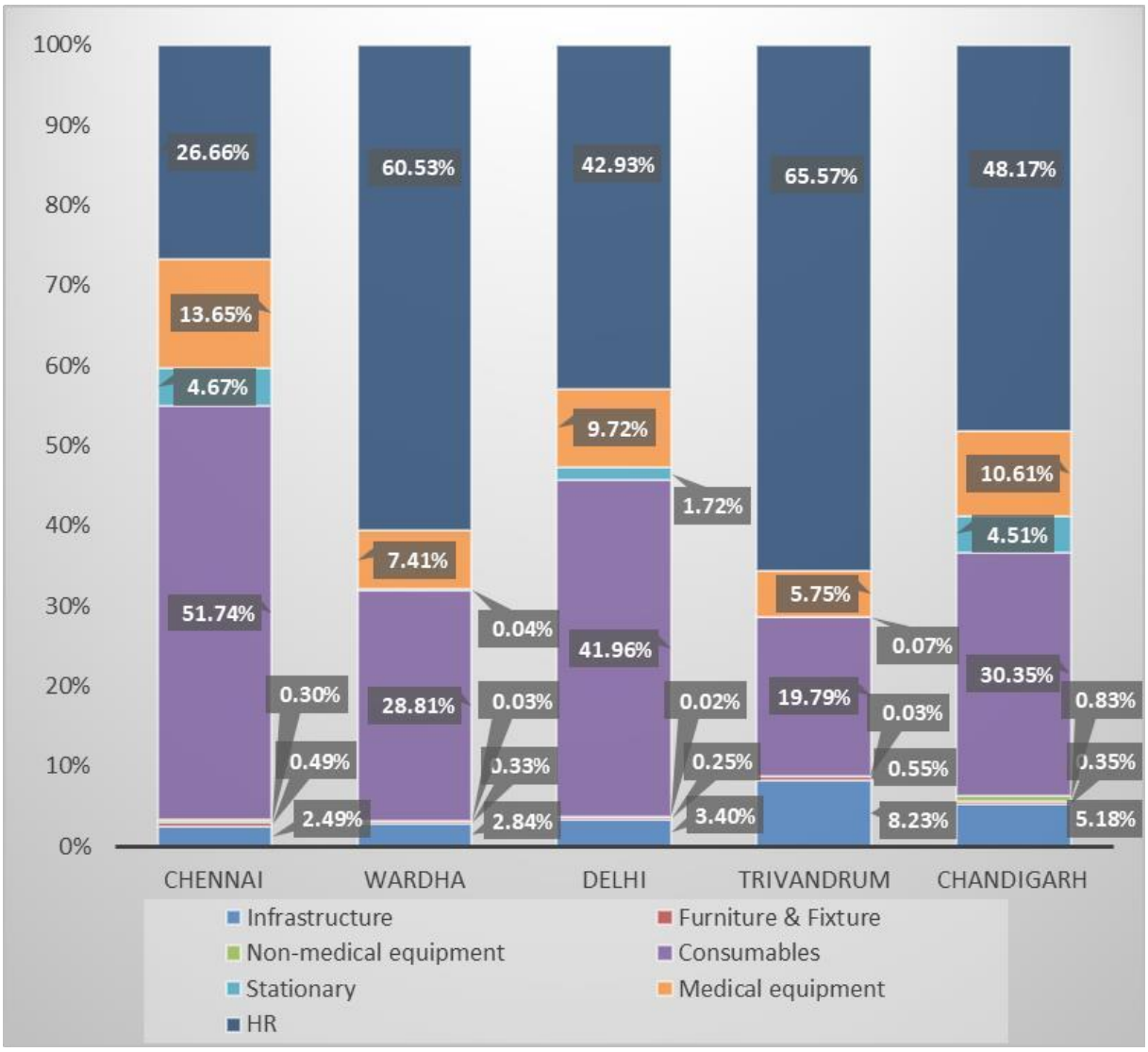
Table 7: Health system cost of IVF cycle using modified approach

Site name	Costs of 1 IVF cycle (without medicines)
PGIMER, Chandigarh	Rs. 61,674
SAT, Trivandrum	Rs. 72,091
MAMC, Delhi	Rs. 52,563
SRM, Chennai	Rs. 43,829
AVBRH, Wardha	Rs. 41,001

The difference in these costs can be justified by varied procurement prices and consumables quantity used in IVF cycles at different sites.

The share of different cost-components in the total cost is depicted in the figure below.

Figure 11: Share of different cost-components in one IVF cycle

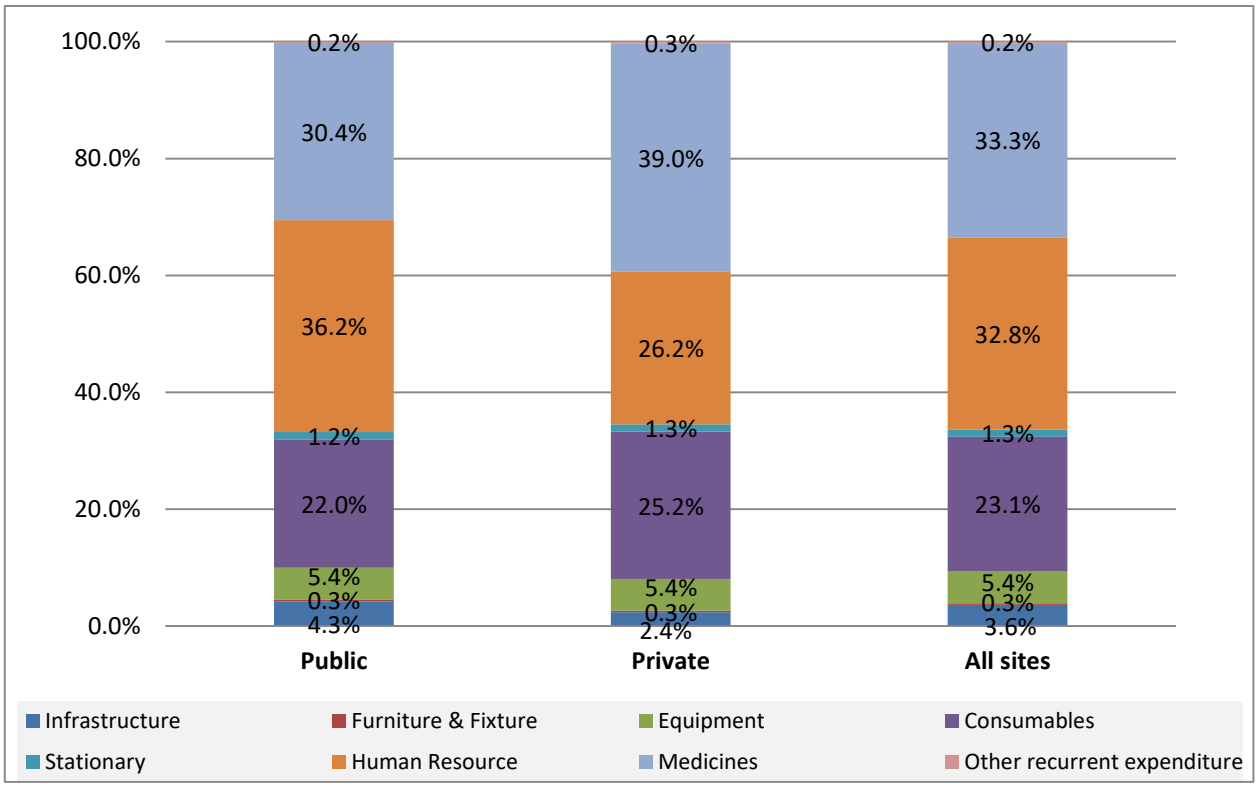


As evident from the figure, expenditure on human resources had the highest share in the total cost at most sites, followed by consumables.

Share of components of Health system cost based on facility type:

The mean cost of one IVF cycle along with medicines for public facility was Rs. 89,209 (+/- 9772) and for private facility was Rs. 69515 (+/- 1999). The difference in cost of private compared to public facilities was due to larger area of facility and additional dedicated staff for IVF in public facilities. The share of various cost components based on the facility type is provided below. In both public and private facility the major cost component is human resource followed by medicines and consumables.

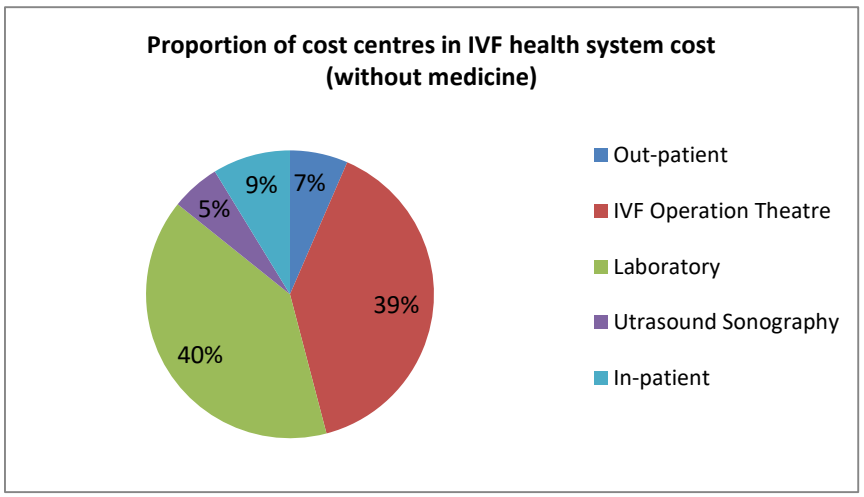
Figure 12: Components of Health system cost based on facility type



Proportion of various cost centres in Health system cost of IVF:

The share of cost centres in health system cost of IVF is provided in the figure below. The share was highest for laboratory followed by OT and IPD.

Figure13. Proportion of cost centres in IVF health system cost (without medicines)



3.2 Analysis of costs and quality of life among couples undergoing diagnosis and management ofInfertility for selected five etiological conditions

3.2.1 Background characteristics of patients undergoing treatment for Infertility:

Participants who were undergoing infertility treatments and diagnosed exclusively for five factors were enrolled. Their out-of-pocket expenditure incurred for diagnosis and management of infertility in the last one year were recorded.

A total of 500 participants were enrolled for infertility, 80% were female factor and 20% had a male factor infertility. Among the female factor, 38 % had PCOS followed by 22% having tubal factor. Azoospermia accounted for 51% of the male factor infertility.

Table 8: Background characteristics (Infertility)

N=500	Male	Female
Age in years (Mean±SD)	34.10 (±4.67)	30 (±4.4)
Education	Illiterate-0% School-8.2% SSC-18.4% HSC-15.3% Diploma-11.2% Graduate-38.8% Postgraduate-8.2% PhD-0%	Illiterate-1.2% School-10.9% SSC-12.9% HSC-22.6% Diploma-3.2% Graduate-37.1% Postgraduate-11.4% PhD-0.5%
Employment	Employed-100%	Employed-17% Homemaker-83%
Married since (years± SD)	6 (±4)	
Years of undergoing infertility treatment (mean ±SD)	4 (±3)	
Number of clinics visited for treatment (mean ±SD)	3 (±2)	
Type of infertility	Primary:73%	Secondary: 27%
Family history of infertility	Male-14%	Female-11%
Tobacco consumption	Male-16%.	Female-0%
Alcohol consumption	Male-33%.	Female-2%
Average monthly family income in INR (Mean± SD)	Rs. 31,828 (±29,700)	
Co-morbid conditions: History of Diabetes: History of Hypertension: History of Hypothyroidism-	 Male:4% Male: 2% Male: 4%	 Female- 2% Female-1% Female-24%

Participants reported that the share of annual infertility expenditure (including IVF) from total household consumption expenditure was 21% (±14%).

Only 1% of the total participants had insurance coverage for infertility treatment and about 44% had obtained financial support by taking personal loans or borrowing from family and friends.

During the study period, out of total participants enrolled, the causes of infertility (from five specific causes) were as below. Majority (38%) were PCOS cases.

Table 9: Causes of infertility among the participants (Infertility)

Factor of infertility	Total number (N=500)	%
Endometriosis	53	10.6%
Tubal block	109	21.8%
Uterine factor	50	10%
PCOS	190	38%
Male infertility	98	19.6%

35% of the total participants had undergone surgeries previously, with most of them having undergone hystero-laparoscopy.

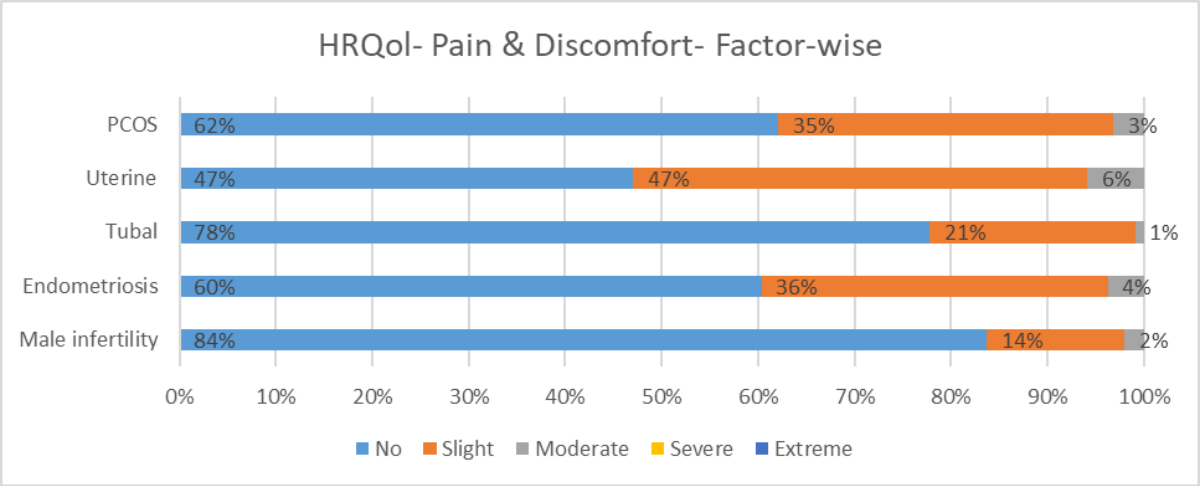
3.2.2 Health-Related Quality of Life-Infertility

Health-related quality of life was assessed using EQ-5D and Visual Analogue Scale (VAS). Utility score of 1 signifies full health. The VAS score ranges from 0 (worst imaginable health) to 100 (best imaginable health). As is evident women who had uterine cause of infertility and endometriosis had a poor utility score. The best scores were for those with tubal factor.

Table 10: Factor-wise utility score and VAS score

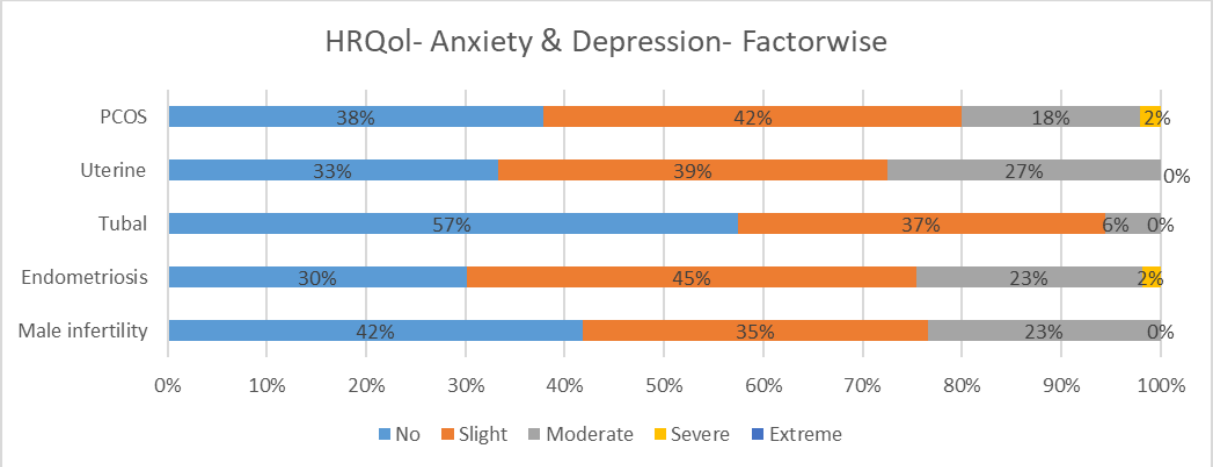
Factor-wise (N=500)	Utility score Mean±SD	VAS Score Mean±SD
Uterine (n=50)	0.93 (±0.08)	76.14 (±18.14)
Endometriosis (n=53)	0.94 (±0.07)	76.3(±17.4)
PCOS (n=190)	0.95 (±0.06)	76.20 (±18.26)
Tubal (n=109)	0.98 (±0.03)	84.9 (±17.4)
Male infertility(n=98) (Male respondents)	0.96 (±0.04)	79.86 (±16.27)

Figure 14: Health-related Quality of Life- Factor-wise: Pain & Discomfort



Out of the five dimensions of HRQOL, majority of the participants reported experiencing pain & discomfort and anxiety & depression, while mobility, self-care, and usual activity were not affected. Amongst the participants having uterine factor infertility, more than 50% have reported having slight to moderate pain & discomfort, followed by endometriosis.

Figure 15: Health-related Quality of Life- Factor-wise: Anxiety & Depression



About 70% of the participants having endometriosis reported experiencing slight to moderate form of anxiety & depression. Severe anxiety & depression were reported by 2% of participants with PCOS and Endometriosis.

3.2.3 Out-of-pocket expenditure (OOPE) incurred by Infertility patients not including IVF

Infertility Treatment Costs borne by patients:

The total out-of-pocket expenditure for infertility treatment for one year for selected factors (Endometriosis, Male Infertility, PCOS, Tubal Factor and Uterine Factor) in India is ₹11317 (IQR: 4801, 19513). This expenditure includes direct medical costs (consultations, medications, procedures), non-medical costs (travel, accommodation and food), and Indirect costs (lost wages due to appointments or recovery).

Table 11: OOPE Expenditure- infertility

Median (IQR: 25%, 75%)	Total (N=500)	Public (N = 300)	Private (N = 200)
Overall Costs	**₹11317** (4801,19513)	₹**7340** (3148,15727)	₹**11834** (6087,19638)
Direct Health Costs (DHC)	**₹5802** (2186,11847)	₹**2636** (1290, 7182)	₹**10137** (5906,16559)
Non-Medical Costs (NMC)	**₹1775** (600, 4000)	₹**2160** (1000, 5200)	₹**1200** (120, 2740)
Indirect Cost (IC)	**₹500** (0, 2705)	₹**4000** (1411, 8000)	₹**1806*** (1032, 3225)

The above table reveals that overall OOPE is higher at private hospitals compared to public hospitals as also the DHCs. However indirect costs are highest among those seeking services from public facilities which is an indirect reflection of the socioeconomic class of patients as they lose their daily wages. Overall indirect cost was reported by only 42.6% of patients. The median cost for NMC in public sector is more as compared to private sector which suggests that patients availing care at public facilities travel far distances from home. So, the patients had to spend more on travelling, food and accommodation.

Table 13 shows overall median expenditure for Endometriosis ₹15084 is highest followed by Uterine Factor (₹13211), Male Infertility (₹13113), PCOS (₹11608) and Tubal Factor infertility (₹7077) being the least expensive. In PCOS only 48% patients and in Tubal Factor only 40% had incurred loss of wage due to treatment.

Table 12: Factor wise distribution of OOPE

Median in INR (IQR: 25%, 75%)	Endometriosis (N = 53)	Male Infertility (N = 98)	PCOS (N= 190)	Tubal Factor (N = 109)	Uterine Factor (N = 50)
Total (N = 500)	**₹15084** (8114, 20758)	**₹13113** (7917, 20698)	**₹11608** (4883, 18741)	**₹7077** (2881, 12219)	**₹13211** (6654, 21521)
Direct Health Costs Median (IQR: 25%, 75%)	Median-**₹** 10607 (3402, 14077)	Median- **₹7034** (4511, 11068)	Median- **₹5566** (2142, 11744)	Median -**₹3303** (854, 7955)	Median -**₹7307** (2822, 15197)
Non-Medical Costs Median (IQR: 25%, 75%)	Median- **₹2000** (1080, 5200)	Median- **₹2040** (806, 4300)	Median-**₹1800** (700, 4530)	Median-**₹1270** (1100, 2712)	Median -**₹1710** (623, 4213)
Indirect Costs Median (IQR: 25%, 75%)	Median- **₹258** (0, 3000)	Median- **₹1903** (0, 3867)	Median -**₹1967*** (967, 5842) Out of 190 only 92 participants had indirect costs	Median -**₹1612*** (824, 3854) Out of 109 participants only 44 participants had indirect costs	Median -**₹1000** (0, 2550)

Intra Uterine Insemination (IUI):

Table 13: Distribution of Costs w.r.t IUI treatment

Median (IQR: 25%, 75%)	Total (N=324)	Public (N = 133)	Private (N = 191)
Overall Costs	**₹14319** (7784, 23763)	**₹7418** (4343, 15333)	**₹12255** (9311, 18290)
Direct Health Costs (DHC)	**₹7874** (4801, 12786)	**₹4155** (2124, 7130	**₹9840** (7508, 15270)
Non-Medical Costs (NMC)	**₹1130** (300, 2400)	**₹1800** (300, 3850)	**₹840** (325, 1700)
Indirect Cost (IC)	**₹1400** (645, 2951)	**₹2500** (1000, 6500)	**₹645** (0, 1612)

64.8% patients had undergone IUI treatment and OOPE is highest for DHC ₹7874 followed by IC ₹1400 and NMC ₹1130. Only 55.2% people had incurred indirect cost due to IUI treatment. As expected, private hospital charges were nearly double than that of public hospital settings.

Analysis revealed that the median share of total OOPE on infertility treatment for one year within the total annual household consumption expenditure was 9% (IQR: 3.9%, 17.1%). However, 43.8% patients undergoing infertility treatment incurred catastrophic expenditure due to the treatment. Out of which 79% and 21% patients were from public and private sector respectively.

3.2.4 Health system costing- Infertility

The cost of management of 5 factors of infertility at public and private sites is depicted in the table below.

Table 14: Health system costing of management of single-factor infertility

Median (IQR: 25%, 75%)	**Cost of 1 year management of infertility in public sector Median (IQR)**	**Cost of 1 year management of infertility in private sector Median (IQR)**
Endometriosis	Rs. 7,503 (5341, 9244)	Rs. 7,773 (7371, 8174)
Tubal block	Rs. 6,650 (4720, 9791)	Rs. 6,673 (5692, 7654)
Uterine factor	Rs. 14,049 (8452,15185)	Rs. 5,988 (4570, 7406)
PCOS	Rs. 12,015 (6801, 12310)	Rs. 6,294 (5494, 7095)

Male infertility	Rs. 6,951 (5305, 8404)	Rs. 5,118 (4421, 5815)

As evident from the results, the cost of infertility treatment for 1 year is lower in public facilities than the private ones, which is likely due to more efficient utilisation of resources in the public sector. The wide range of cost is due to variations in the management of patients based on aetiology of infertility.

Additional costs:

The cost of one cycle of IUI without medicines ranged of Rs. 7,676 and Rs. 8,247. For patients undergoing IUI, this will be an additional health system cost for infertility treatment. Among the study participants, 16% of all tubal block patients underwent tuboplasty as part of infertility management. For them, the additional cost of surgery along with IPD days comes at Rs. 11,904. For uterine factor, 12% of patients underwent myomectomy, which will amount to an additional cost of Rs. 16,347. Around 12% of patients with PCOS underwent laparoscopic ovarian drilling, which will lead to additional cost of Rs. 13,008.

These results should be seen with the results of IVF costing. The treatment of infertility including IUI is less costly to the health system compared to technologically advanced and costlier IVF. With increasing focus and demand of IVF, there is a need to focus on infertility services as well to optimally utilise resources and reduce the overall economic burden of infertility management in the country.

Chapter 4: Conclusions, Recommendation and Implications

4.1 Conclusions

4.1.1 IVF

- Majority (88.5%) of patients undergoing IVF had incurred catastrophic expenditures due to the treatment.
- Around 5% of the participants had insurance coverage for IVF treatment. An average of Rs. 100625 (±35,500) of the treatment expense was covered by insurance.
- Just over half (58 %) of the total participants had obtained financial support of which 60% had borrowed from friends and family while others had taken bank or gold loans.
- The quality-of-life measures for couples undergoing IVF further reduced compared to the ones who were not receiving IVF. In males, utility score reduced by 0.01 and in females by 0.04 while undergoing IVF. Pain/discomfort and Anxiety/depression contributed to poor quality of life in wives while husbands had poor scores in the dimension of anxiety/depression.
- The average OOPE of participants undergoing IVF treatment at public hospitals was Rs. 1,09,671 and Rs. 2,30,668.5 for private hospitals respectively.
- The direct health cost comprised mainly of expenditure on investigations and medicines in public sector while in private sector this component included expenditure on procedures, investigations and medicines. The direct health expenditure for one IVF cycle at public and private sites is respectively Rs. 92,358 and Rs. 2,12,744. Providing IVF reimbursement under PM-JAY will significantly reduce this financial burden of the patients.
- The health system cost of providing one IVF cycle including costs of medicines irrespective of the facility's operational efficiency is Rs. 81,332 (+/- 12,849).
- The health system cost derived for providing one IVF cycle is in line with the ART Act 2021.

4.1.2 Infertility

- One fourth (25%) patients undergoing infertility treatment incurred catastrophic expenditure due to the treatment. Out of which 62% patients from public sector and 38 % patients from private sector.
- Less than half (44%) of the participant couples had obtained financial support in the form of borrowing or loans to pay for infertility treatment.
- Patients with uterine factor infertility and endometriosis had the lowest Health-Related Quality of Life. Pain/discomfort and anxiety/depression were the dimensions contributing most to the poor quality of life of the patients.
- The health system cost of infertility management for one year in the public facilities ranges between Rs. 6,822 to Rs. 11,075 for 5 different factors of infertility. The cost is higher in the private than public facilities.

4.2 Recommendations

- Based on study findings, the IVF package for consideration under Pradhan Mantri Jan Arogya Yojana (PM-JAY) could be considered at Rs. 81,332 for one IVF cycle.
- Currently, OPD expenses are not covered under PM-JAY. As the majority of expenditure for infertility treatment including IVF is OPD based, this consideration needs to be made for including IVF in the PM-JAY package.
- Since nearly 44% of couples undergoing infertility treatment face catastrophic expenditure, this cost could also be considered for reimbursement under PM-JAY.

Number of IVF cycles to cover through PMJAY:

In 2011 CGHS had issued an order to reimburse upto 3 cycles of IVF [8]

According to NICE guidelines, 3 cycles of IVF are offered to women under 40 who have not conceived after 6 or more cycles of IUI [13]

- In view of the above, PMJAY could consider including 3 cycles of IVF for reimbursement.

4.3 Implications:

The findings from this study could be used for conduct of Cost-effectiveness studies on IVF or infertility management.

We propose to extend the study to conduct cost-effectiveness analysis on the following topics:

1. GnRh antagonist conventional protocol versus minimal stimulation for ovarian stimulation in IVF

2. Clomiphene citrate versus letrozole in treatment of infertility due to PCOS in public healthcare settings

3. Cost-effectiveness analysis of oral versus injectable gonadotropins for controlled ovarian stimulation in infertility treatment due to PCOS

3. Cost-utility analysis of ulipristal versus leuprolide in treatment of infertility due to uterine fibroid in public healthcare settings

4. Cost-effectiveness of three versus six IUI cycles before IVF

5. Cost-effectiveness of fresh versus frozen embryo transfers for IVF

4.4 Budget Impact Analysis for IVF:

The budget impact analysis was undertaken to identify the total monetary budget needed by the public health system to provide IVF services to the entire cohort. The population of women with infertility among those married more than 5 years was identified. The burden of infertility was used from a study by Agiwal et al. which assessed the prevalence of primary infertility at both national and state levels in India Employing data from the National Family Health Survey-5 (NFHS-5, 2019–21). The findings showed that the prevalence of infertility is 18.7 per 1,000 women among those married for five or more years [(14)]. As per the expert 10% of the women with infertility will undergo IVF treatment. From the census 2011 for married women for five years or more between 15-49 years was population data was obtained. Using the projected population for 2023, the population of women married for five years or above was estimated for year 2023. The estimated cohort of infertile female married for 5 years of age 15-49 years and opting for IVF was 3,32,381 [(15,16)]. The following tables specifies the input and the Budget estimates.

Table 15: Estimated Budget Impact for providing IVF in India

Population Parameter	Value
Prevalence of infertility in 1000 female[(14)]	18.7 per 1000
15-49 years of women more than 5 years of marriage estimated for 2023 based on projection report	17,77,43,895
Total number of women with infertility	33,23,811
Women opting for IVF (10% of infertility)	3,32,381
Cost Parameters	**Value (INR)**
Mean package cost of one IVF cycle including medicines	81,332
Total Cost of IVF for the cohort	**27,03,32,18,285**
Total Budget IVF (in crores INR)	**2,703 crores**

The Health system package to provide one IVF cycle was Rs. 81,332 (±12,949). The total budget estimates for providing IVF services in India as per the cohort is estimated to be Rs. 2,703 crores.

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