# SPERM DNA FRAGMENTATION: CAUSES, EVALUATION AND MANAGEMENT IN MALE INFERTILITY

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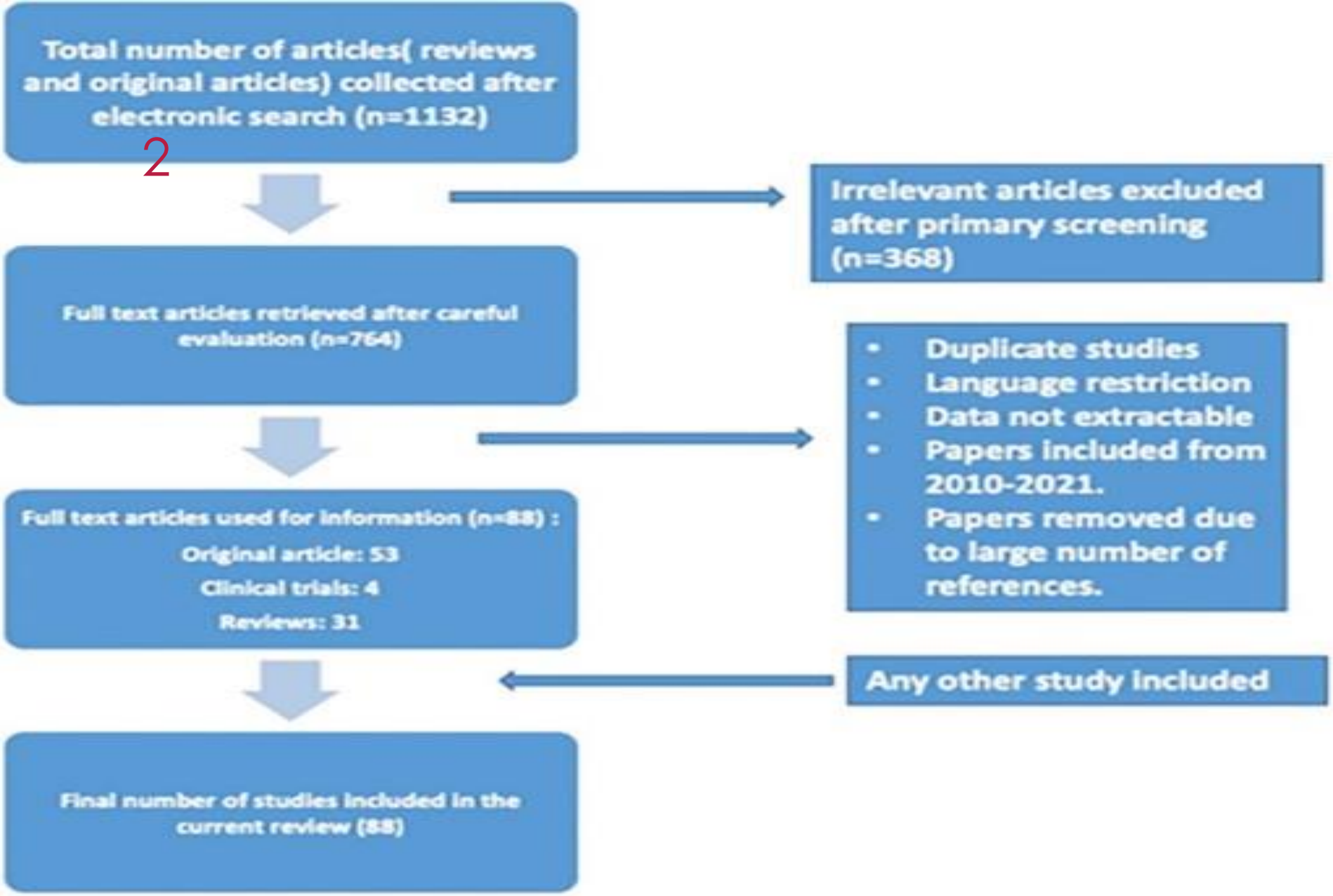

Total number of articles( reviews and original articles) collected after electronic search (n=1132)
2
Irrelevant articles excluded after primary screening (n=368)
Full text articles retrieved after careful evaluation (n=764)
Duplicate studies
Language restriction
Data not extractable
Papers included from 2010-2021.
Papers removed due to large number of references.
Full text articles used for information (n=88) :
Original article: 53
Clinical trials: 4
Reviews: 31
Any other study included
Final number of studies included in the current review (88)

# 3 TOPICS

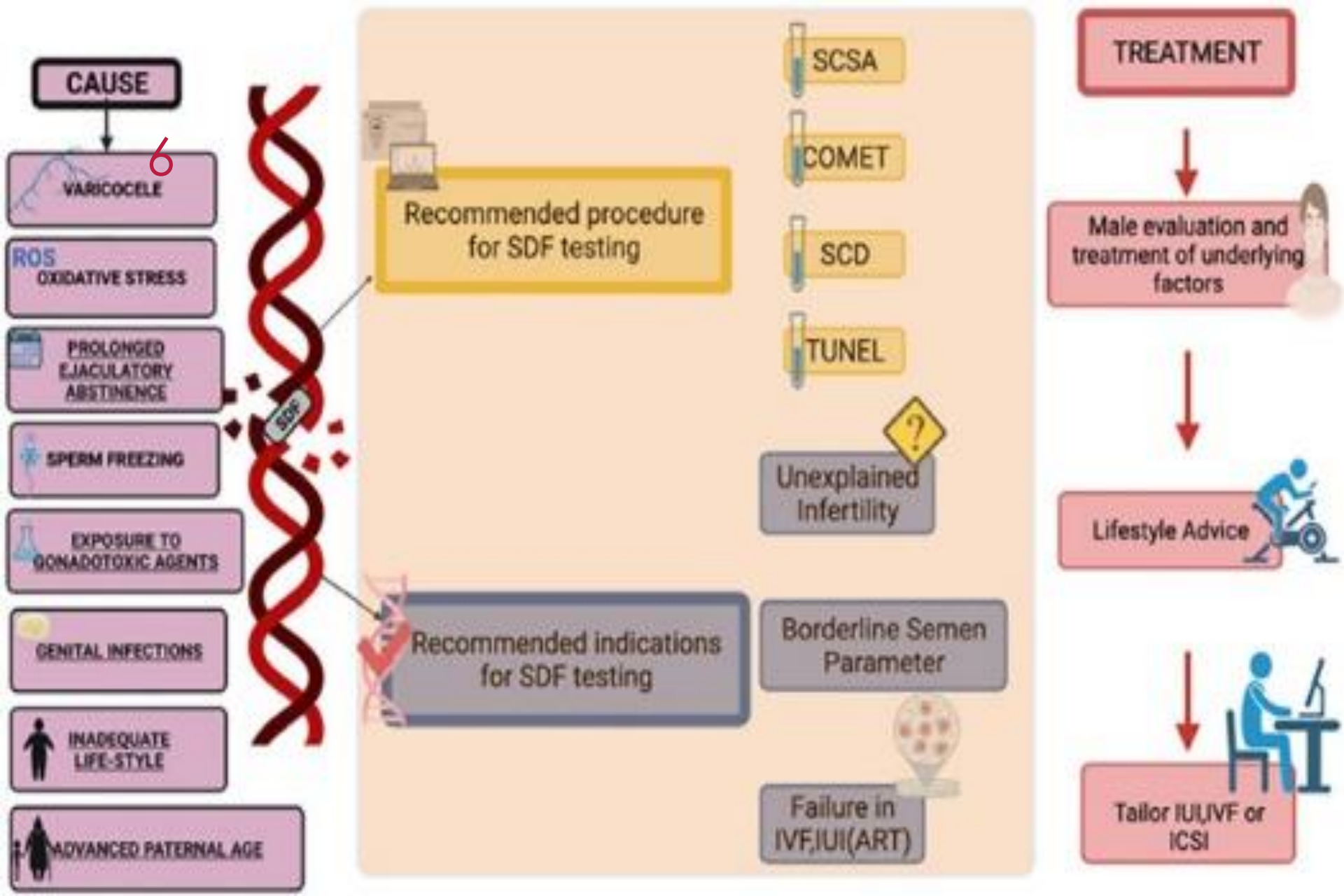
- Introduction
- Causes of SDF
- Intrinsic factors
- Extrinsic factors
- Impact of SDF
- SDF testing when?
- Treatments and prevention
- Conclusion
- References

# 4 INTRODUCTION

- Sperm DNA fragmentation has been reported to be associated with male infertility and productive failure
- SDF also results in impaired fertilization,sub-optimal embryo quality,reduced pregnancy rate and increased abortion during IVF.

# 5 CAUSES OF SDF

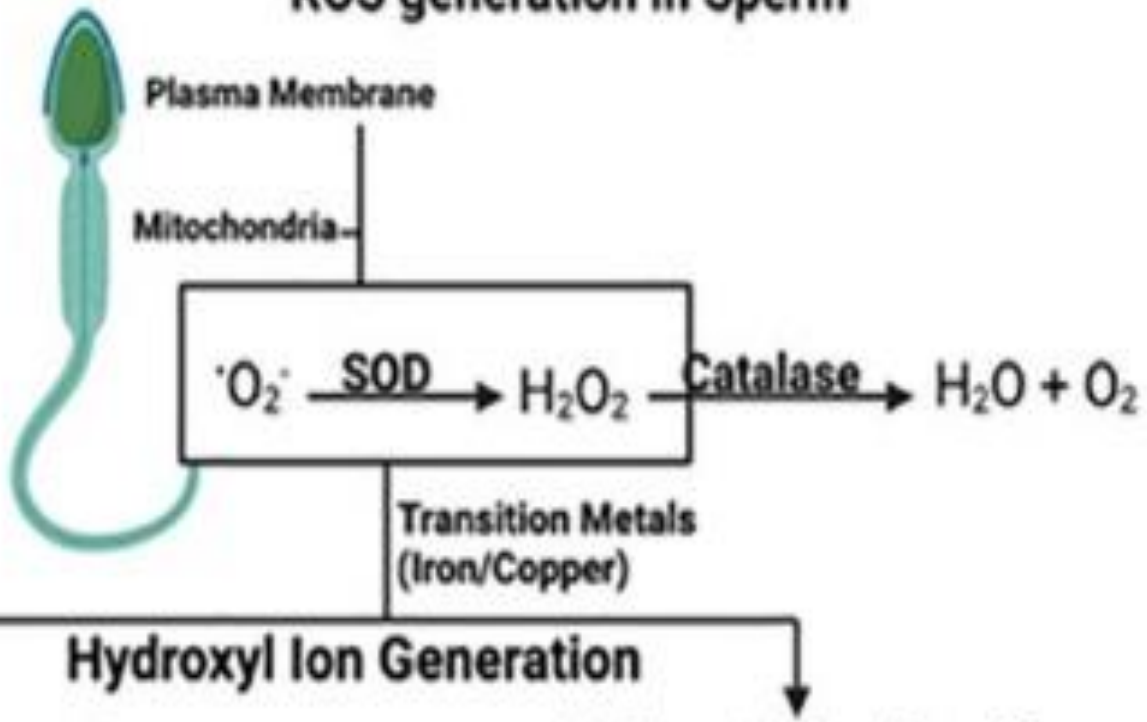
- 1.Abnormal chromatin packaging and remodeling during spermatogenesis
- 2.Apoptosis during epididymal sperm maturation
- 3.oxidative stress
- 4.Varicocele, infections, inflammation of male genital tract, febrile illness, obesity, advanced age, environmental pollutants and toxins
- 5.Drugs, chemotherapy and radiotherapy


CAUSE
6
VARICOCELE
ROS
OXIDATIVE STRESS
PROLONGED EJACULATORY ABSTINENCE
SPERM FREEZING
EXPOSURE TO GONADOTOXIC AGENTS
GENITAL INFECTIONS
INADEQUATE LIFE-STYLE
ADVANCED PATERNAL AGE
SDF
Recommended procedure for SDF testing
SCSA
COMET
SCD
TUNEL
Unexplained Infertility
Recommended indications for SDF testing
Borderline Semen Parameter
Failure in IVF,IUI(ART)
TREATMENT
Male evaluation and treatment of underlying factors
Lifestyle Advice
Tailor IUI,IVF or ICSI

# 7 INTRINSIC FACTORS

- A.Recombination deficiencies during spermatogenesis
- B.abnormal spermatid maturation
- C.Protamine 1 and 2 ratio
- D.oxidative stress
- E.Varicocele(due to ROS and venous stasis)(grade 2-3)
- F.Genital tract infections
- G. Age

# ROS generation in Sperm



# 9 EXTRINSIC FACTORS

- A.Abstinence period
- C.Storage Temperature and Cryopreservation
- D.Heat stress ,tobacco,smoking,Cadmium, antidepressant drugs
- E.other factors

# 10 IMPACT OF SDF

- 1.SDF and Male infertility
- 2.SDF and natural pregnancy outcomes
- 3.SDF and Different ARTs (IUI, IVF, ICSI)
- 4.SDF and birth defects

**Table 1.** Clinical impact of abnormal SDF level.

| Clinical Scenario | Remarks | Study |
|---|---|---|
| Unexplained infertility | 20% of men with unexplained infertility and 40-50% of men with idiopathic infertility have abnormal SDF. | Esteves *et al.*, 2020<br>Gill et al., 2019 |
| Recurrent Pregnancy loss or pregnancy loss | >30% SDF level was found critical for pregnancy outcomes. In-case of recurrent pregnancy loss SDF level was elevated after natural or assisted conception | Tan *et al.*, 2019<br>Esteves *et al.*, 2021 |
| Failed IUI | Abnormal SDF negatively affect pregnancy rates in IUI | Sugihara *et al.*, 2020 |
| Failed IVF/ICSI | Abnormal SDF affect IVF/ICSI pregnancy rate. Men with high SDF on ICSI with testicular sperm gave better pregnancy result. | Esteves & Roque, 2019<br>Xie *et al.*, 2020 |
| Abnormal embryo development and birth Defects | SDF adversely affect embryo development. Icsi patient having high SDF had high aneuploidy and genomic abnormalities | Kim *et al.*, 2019<br>Zheng *et al.*, 2018 |

# 12 SDF AND MALE FERTILITY

- high SDF can act as a barrier to male fertility
- SDF was categorized into viable and non-viable

# 13 SDF AND NATURAL PREGNANCY OUTCOMES

- 20-30% SDF level:decreased natural pregnancy chance
- more than 30% SDF level : critical
- 30% of cases with SDF higher than 15% had recurrent miscarriages

# SDF AND DIFFERENT ARTS, SDF AND BIRTH DEFECTS

- 3. SDF and different ARTs(IUI,IVF,ICSI)
- The inability to conceive increased in couples having SDF levels higher than 30% compared to couples with SDF levels lesser than 10%.
- 4. SDF and birth defects:
- A link between males with high sperm DNA damage and genetic abnormalities in offspring.
- Increased aneuploidy and genomic abnormalities associated with an increase in SDF level undergoing ICSI treatment.

# 15 SDF TESTING,WHEN?

- In 2017: Agarwal et al:

Specific guidelines for SDF testing

1.Unexplained infertility

2.Varicocele(grade 2-3 with standard semen parameters)

3.RPL

4.Unexplained ART failure(more discussed in IVF)

5.Exposure to lifestyle risk factors

# 16 TREATMENT AND PREVENTION

- Lifestyle changes
- Antioxidant therapy
- Varicocelectomy
- Short abstinence
- Use of testicular sperm for ICSI
- Sperm processing andselection media and devices

# 17 LIFESTYLE CHANGE

- 1. Lifestyle improvement
- (BMI) along with metabolic syndrome (MetS)
- Nutraceutical having myo-inositol, alpha lipoic acid, coenzyme Q10, Selenium, zinc and vit B may affect idiopathic infertile men

# 18 LIFESTYLE CHANGE

- Break of smoking and drinking habits+ exercise and weight loss
- Stress:behavioral cognitive therapy,meditation and behavioral therapy
- Sleeping cycle should be examined.
- Three months lifestyle intervention program which included diet and exercise was done on patients having DFI>15%. Reduced median DFI from 25.8% to 18% was seen after intervention

# 19 ANTIOXIDANT THERAPY

- still debatable.
- High ROS levels causing base modification, strand break, and cross link chromatin.
- vitamin A, C, and E+ micronutrients like L-carnitine, N-acetyl cysteine,zinc and selenium
- CoenzymeQ
- Three months of oral anti-oxidant therapy having multivitamins, coenzyme Q10, omega-3 and oligo-elements was done decreasing mean DFI to 7.2% in 31 participated patients having DFI>15%

| Vitamin C | Vitamin E | Zinc | Seleniu |
|---|---|---|---|
| Papaya | Spinach | Spinach | Halibut |
| Bell peppers | Swiss chard | Shiitake mushroom | Tuna |
| Strawberries | Sunflower seeds | Cremini mushroom | Cod |
| Broccoli | Almonds | Organic Lamb | Shrimp |
| Pineapple | Asparagus | Organic Beef | Cremini mushroc |
| Kiwi | Bell peppers | Scallops | Mustard seeds |
| Oranges | Cayenne Pepper | Sesame Seeds | Sardines |
| Cantaloupe | Papaya | Pumpkin seeds | Salmon |
| Kale | Kale | Oats | Turkey |
| Cauliflower | | | barley |

# 21 VARICOCELECTOMY

- C. Varicocelectomy
- Reduced SDF levels along with increased pregnancy rates were found post 1-year of varicocelectomy.
- study conducted post-varicocelectomy showed reduction in SDF levels from 35.2% to 30.2% resulting in 37% of patients conceived naturally and another 24% by ART

# 22 SHORT ABSTINENCE

- A 22.25% DNA damage was found to be improved when the abstinence period was around 1-2 days
- In another study,by reducing the abstinence period to one day, 91.4% males showed low SDF levels (<30%)

# USE OF TESTICULAR SPERM FOR ICSI

- has been found that testicular spermatozoa have much better DNA quality than ejaculated sperm (3-5-fold)
- showed a positive rise in ICSI in oligozoospermic with high DFI levels

# 24 SPERM PROCESSING AND SELECTION MEDIA AND DEVICES

- During ART, sperms get isolated by different procedures of sperm selection
- including
- density gradient centrifugation,
- intracytoplasmic morphological sperm selection (IMSI),
- electrophoretic isolation,
- physiological ICSI (PICSI) dishes,
- hyaluronic acid binding assay like Sperm-Slow and magnetic cell sorting (MACS)

# 25 CONCLUSION

- Certain factors lead to sperm DNA fragmentation through spermatogenesis.
- Rise of SDF level  is considered as a cause of infertility.
- SDF testing is recommended in certain patients.
- SDF treatment and prevention: from conservative treatment to methods such as varicocelectomy and ART techniques.

# 26 REFERENCE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# THANKS FOR YOUR ATTENTION