ASSOCIATION OF HORMONAL IMBALANCE, LIFESTYLE AND CLINICAL ATTRIBUTES WITH FEMALE INFERTILITY.

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ABSTRACT

OBJECTIVE: Millions of couples are affected by infertility annually due to several reasons throughout the world. The aim of present study was to evaluate the association between female infertility, hormonal imbalance, lifestyle and clinical attributes. **METHODS:** The females suffering from infertility were evaluated through different parameters, including hormones (FSH, LH, TSH and Prolactin) diet, weight, age, workload, emotions, habits and transvaginal scans (TVS).The findings were compared between fertile and in infertile women. **RESULTS:** The participants included in this study were 110 infertile females, age 18 to 40 (Mean age ± SD 29 ± 6.78) years. The major group of infertile females (45.5%) was aged 18 to 27 years. Overall 85.5% females were housewives with 79% literacy rate, and the majority of females were either overweight (48.2%) or obese (21.8%). About half of infertile females were very frequently eating junk food including chicken and meat and thus 41.8% of the female got irregular menstrual cycle due to hormonal disturbance. An important association between the level of follicle stimulating hormone, leutinizing hormone, Prolactin, the reproductive age and female's infertility was observed. About 68-70% infertile females showed imbalance of FSH and LH from borderline to abnormal while TSH and Prolactin were 37-42% from borderline to abnormal. In TVS, 86.4% females showed immature and multiple small sized follicles which were failed to mature enough for ovulation. **CONCLUSION:** The present research concluded that female diet and lifestyle also play a major role in fertility. The hormonal imbalance for LH, FSH, TSH and Prolactin is significant assumption which causes infertility problem in the studied patients.

KEYWORDS: Infertility, Transvaginal Scan, Hormonal Imbalance

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INTRODUCTION

Infertility is an inability of a couple to conceive a pregnancy after one year of marriage [1]. Every year millions of couples are affected by either female infertility, male infertility or infertility from both male and female partner throughout the world. Probably 60-80 million couples experience infertility each year [2]. Female fertility is at its peak between the ages of 18 and 24 years, while, it begins to decline after age of 27 years, and drops at a somewhat greater rate after age 35 years [3]. Childlessness is not just a fitness issue; it is also a topic of public intolerance and differences. However, it appears that the woman is consistently held responsible for a couple's infertility, as a result she is often punished emotionally and socially [3]. There are several reasons for female infertility; it causes due to lack of ovulation, blocked fallopian tubes, endometriosis or uterine abnormalities. Genetic abnormalities, hormonal imbalances, congenital genital abnormalities and infections are among the common reasons for infertility [4]. Weight loss and excessive weight gain can also cause infertility, over weight has been reported to disturb the curing efficiency to achieve pregnancy [5]. Several lifestyle issues may affect reproduction, including routine of taking food, type of food, weight, work load, wearing objects, daily work out, and the use of addiction, any contact to industrial chemical has been also linked with fertility problems [6]. There is a complex connection between sexual activities and infertility; Sexual

dysfunction can also cause a delay in conception [7]. Recently, hormonal disturbances have been greatly considered in causing female infertility. An increase in FSH in women may indicate a reduction in the production of good quality eggs and embryos for fertilization [7]. The fertilization process is not accomplished unless ovarian follicles reach to its proper size from 12–19 mm on the day of trigger following the proper release of hCG, GnRHa, or kisspeptin hormones [8]. Therefore scientists are taking great entrust in in-vitro maturation (IVM) of human immature follicles [9]. This technique is also useful for those females who are not receiving menstrual cycle every month [10]. Female menstrual cycle drive through several hormones in which LH (luteinizing hormone) and FSH (follicle-stimulating hormone) are the most important and work in group. When estrogen level rises up, FSH production discontinues and pituitary gland begins to release more LH which causes mature follicles to be released from the ovary, hence ovulation done. An abnormal release of LH and FSH may be a sign of abnormal ovaries. High levels of LH may take young female to the early puberty stage, whereas less concentration of LH in the blood may be evidence for anorexia, a problem in the pituitary gland because of stress, or upset hypothalamus [11]. Prolactin is another important hormone that participates in the reproductive fitness of couple. The function of prolactin is to start lactation after child delivery on other hand this hormone also creates to measure the sexual desire in married couple [7]. However the hormonal imbalance can be considered as a slight problem of infertility in the female as hormones can bring into balance through providing medication [12].

MATERIALS AND METHODS

Study design

In this study, 110 infertile and 50 fertile women were recruited by collaboration with Umm-e-Majida infertility clinic, Hyderabad and Centre of reproductive medicine of Rehman medical Institute Peshawar. After identification of the patient, written consent was taken from all recruited participants, their partners and parents/guardians. The demographic anthropometric measurements were collected using an authenticated questionnaire containing the information about to the causes of infertility, period of infertility, education, occupation, diet, weight, age, workload, emotions habits, trans-vaginal scan and lifestyles. Clinical investigations for hormones (FSH, LH, TSH and Prolactin) were also carried out. Prior ethical approval was obtained from the university ethical review committee.

Statistical analysis

The statistical analysis was carried out by SPSS 20.0 (SPSS Inc., Chicago, II., USA). On the whole distributed data were articulated as mean ± SD and were evaluated using the t-test; categorical variables were expressed as percentage, cumulative frequency, relative frequency and were compared using the chi-square test as suitable. In the statistical analysis $P < 0.001$ was considered as significant.

Ethics approval

This study is approved by the institutional committee of Biotechnology and Genetics University of Sindh Jamshoro Pakistan under (reference # 122).

RESULTS

The present study included 110 infertile female, the majority of the patients were from urban regions (66.4%), while most of the recruited females were housewives (85.5%), and have normal work load (45.5%). The majority of patients were either overweight (48.2%) or obese (21.8%), due to consuming junk food, chicken and meat mostly. The literacy rate showed, only 40 of infertile female obtained the secondary level of education 23 were illiterate out of 110 infertile females (Table 1).

Out of 110 infertile females 58.2 % females were receiving menstrual cycle regularly, whereas 41.8% females were having menstrual cycle at an abnormal interval which showed insignificant difference among infertile females. The most noticeable finding of present study is follicles size, the TVS ultrasound showed the significant difference in the follicle size of infertile females, Fig: 1-A showing the immature follicle in right ovary, similarly fig 1-B is showing the polycystic ovary. There are number of small size immature follicles in both ovary of the patient, which are unable to fertilize and grow further. On the other hand fig 1-C exhibits the normal follicle which further grow to become a mature follicle and become competent to get fertilized with healthy sperm unveil in fig1-D. Regression Line and Equation between follicles size and age for the studies infertile women showed 86.4% infertile females were having immature follicles during reproductive age (Fig: 2). These small size immature follicles fail to get fertilized. However the reproductive hormonal level was also found disturbed. Total of 24.5 % infertile females were having abnormal FSH, 28.2 % infertile females had abnormal LH, 16.4 % infertile females had abnormal TSH and 18.2% infertile females had abnormal Prolactin mention as shown in table 2. The mean and standard deviation of FSH, LH, TSH, and Prolactin is not showing any major variation of the studied infertile females who were categorized in accordance of age, menstrual cycle, follicles maturity and duration of infertility, enlisted in table 3 P value is also showing insignificant difference but there is the significant differences in follicles maturity in the ovary of infertile females as shown in table 2. The frequency polygon was constructed

by taking the average value of FSH, LH, TSH, and Prolactin in three groups of age in which infertile females were divided. The graphs showed that the level of FSH and Prolactin is decreasing as the age is increasing whereas level of LH and TSH increases as age increases. (fig: 3)In present findings, the maximum number of the studied women got immature follicles, which are unable to fertilize and become a reason of infertility; this may be due to chicken consumption and disturb eating and sleeping routine in their lives which causes hormonal imbalance for (LH, FSH, TSH and Prolactin). it is documented that FSH release raise with increasing age, as Prolactin concentration a little reduce with increasing age. Hence late marriages can be considered as another reason of infertility. consuming ealthy and proper diet can avoid childlessness. The remedial and social support of infertile women is essential to help in overcoming the problem. There are numbers of doors which can be knocked to cure female sterility such as medicines, minor surgery, laparoscopy, hormonal treatment.Fig: 1-A showing the immature follicle in right ovary, similarly fig 1-B is showing the polycystic ovary. There are number of small size immature follicles in both ovary of the patient, which are unable to fertilize and grow further. On the other hand fig 1-C exhibit the normal follicle which further grow to become a mature follicle and become competent to get fertilized with healthy sperm unveil in fig1-D. Maintaining a healthy lifestyle, maintenance of normal body weight, early marriages and

Table-1: Distribution of studied infertile patients in frequency, percentage, P-value and Chi-sq

Sr. n	Attributes	Groups	Age mea	Freq. (n = 110)	%	P value	Chi –sq
1.	Age (Years)	18-27	22.5	50	45.5	0.001	15.13
		28-33	30.5	42	38.1		
		34-40	37	18	16.4		
2.	Residence	Urban		73	66.4		
		Rural		37	33.6		
3.	Occupation	Work		10	9.0	0.00	134.69
		House Wife		94	85.5		
		Student		6	5.5		
4.	Work Load	Less		29	26.4	0.03	7.33
		More		31	28.2		
		Normal		50	45.5		
5.	BMI	Under Weight		3	2.7	0.00	46.14
		Normal		30	27.3		
		Over Weight		53	48.2		
		Obese		24	21.8		
6.	Food	Chicken & Meat		53	48.2	0.00	22.38
		Vegetable		14	12.7		
		Both		43	39.1		
7.	Literacy Rate	Illitrate		23	20.9	0.00	18.94
		Primary		36	32.7		
		Secondary		40	36.4		
		High		11	10		

Table-2: Distribution of studied infertile patients according to regular menstrual cycle, follicle size and leve FSH, LH, TSH and Prolactin.

Sr. n	Hormonal attribute	Groups	Freq. (n = 110	%	P value	Chi –sq
1.	Periods	Regular	64	58.2	0.09	2.94
		Irregular	46	41.8		
2.	Follicles	Mature	15	13.6	0.00	58.18
		Immature	95	86.4		
3.	FSH	Normal	33	30	0.02	7.76
		Borderline	50	45.5		
		Abnormal	27	24.5		
4.	LH	Normal	36	32.7	0.37	1.98
		Borderline	43	39.1		
		Abnormal	31	28.2		
5.	TSH	Normal	69	62.7	0.00	43.11
		Borderline	23	20.9		
		Abnormal	18	16.4		
6.	Prolactin	Normal	63	57.3	0.00	29.04
		Borderline	27	24.5		
		Abnormal	20	18.2		

Table-3: The mean and standard deviation of the concentration of FSH, LH, TSH and Prolactin in patients' groups classified according to age, menstrual cycle, follicles and duration of infertility.

Sl	Attributes	Groups	FSH	LH	TSH	Prolactin
1.	Age (Years)	18-27	8.07±7.5	8.08±9.00	2.11±1.0	24.75±10.08
		28-33	7.72±3.5	16.17±20.8	2.47±1.6	25.21±11.31
		34-40	7.63±4.4	18.68±31.7	2.50±1.2	23.68±8.50
2.	Menstrual Periods	Regular	7.84±4.8	13.14±19.1	2.66±2.0	25.09±11.00
		Irregula	7.81±7.0	13.76±19.4	2.43±1.2	26.78±14.43
3.	Follicles	Mature	7.71±3.0	11.61±14.6	2.37±0.9	29.93±11.05
		Immatur	7.88±6.2	13.68±19.8	2.61±1.8	25.33±12.68
4.	Duration of Infertility (Year	1-5	7.53±6.5	12.04±14.2	2.72±2.0	26.86±14.27
		6-10	8.20±5.5	17.09±28.9	2.02±0.8	23.17± 8.57
		11-15	8.61 ±2.4	10.28 ±4.2	3.26 ±1.9	23.66± 3.90

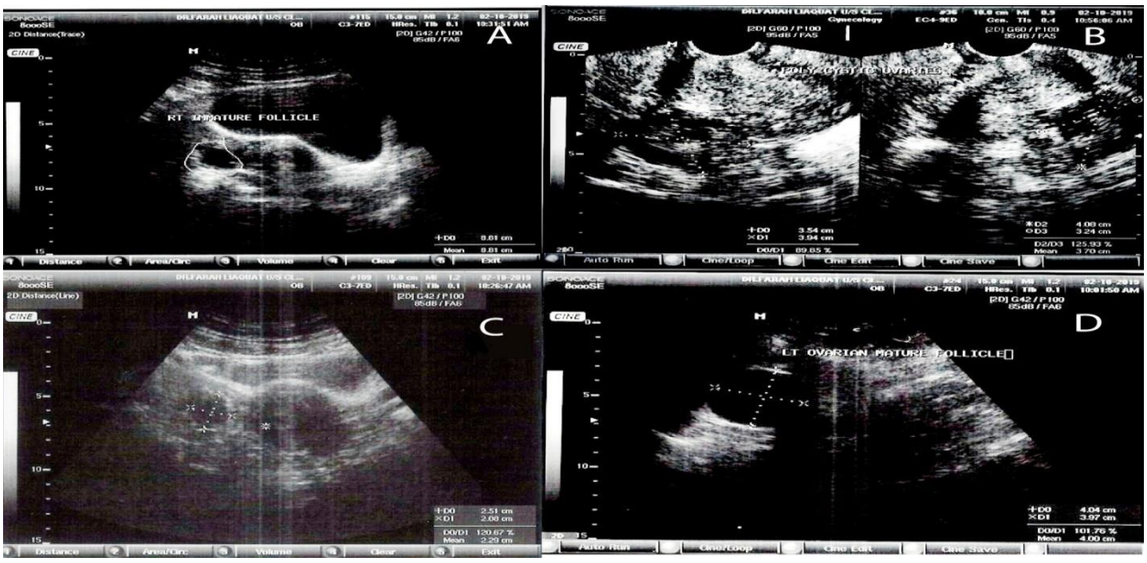

Figure 1: Trans vaginal scan of infertile females

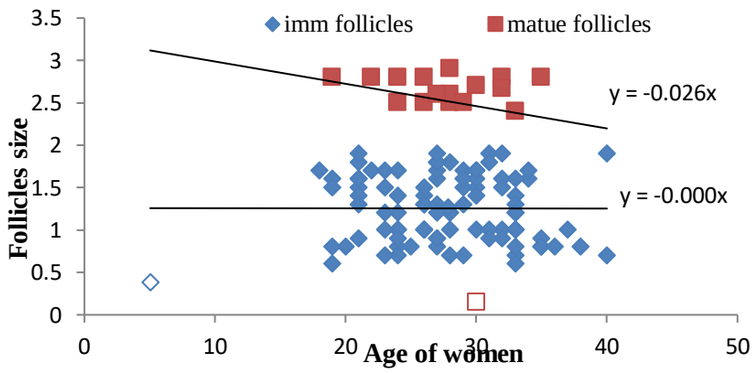

Figure 2: Regression Line and Equation between follicles size and age for the studies infertile women

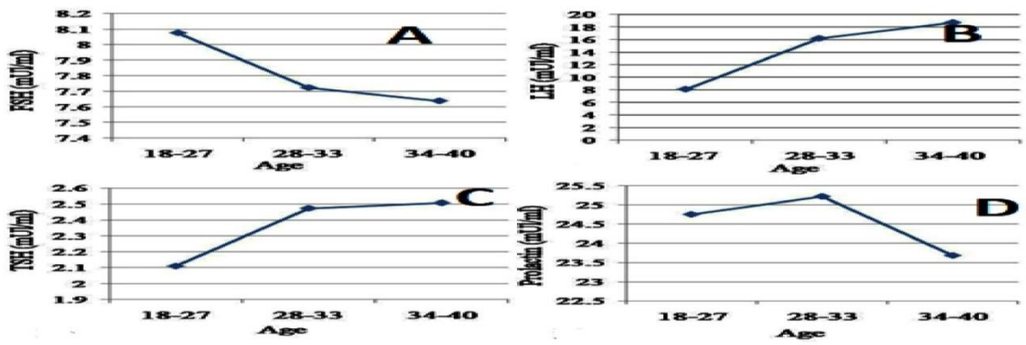

Figure 3: The frequency polygon between the age and the level hormones in females; 1A– age and the level of FSH, 1B – age and the level of LH, 1C – age and the level of TSH, 1D – age and level of Prolactin

DISCUSSION

Infertility may occurs due to various health issues such as oocytes immaturity, blockage in fallopian tube, delay in childbearing, late ages marriages in, weak endometrial lining of uterus, hormone imbalance and the way of living followed by the married couple, stress, non-conducive legal structure for help out reproduction, etc [13]. We found that the maximum numbers of infertile female were from urban areas, and among them there were majority of housewives. Despite the fact that many studies showed that less infertile housewives were found as compared to worker infertile women in urban area [14]. Fertility rates are higher in rural women than urban women with no education [15]. It is reported that increased attendance of higher level of education could have overdue access into marriage and also lift up the probability of using deliberate prevention of conception. This confirms the nation that improvement in education of women is involved in decreasing fertility [2, 16,17]. This agreed the present research that women get married in late ages mostly face infertility issue in their lives, on other hand, some research partly disagrees and stated that spending more years of reproductive age in getting education had no effect on fertility change [18]. The BMI of female should not be greater than 27 kg/m2 in reproductive age as ovaries of fatty or underweight female does not function properly [19]. Overweight has also been found to show negative consequence on curing results and effect of given fertility technique. In fatty people, fat cells produce excessive amount of estrogen together with primary sex organs also release estrogen and thus, state of high body fat or obesity causes increase in estrogen, resulting the reproductive system of female get disturbed, reduces the possibility of pregnancy [20]. In present study most of the studied women were either overweight or obese, it is already reported that obesity and overweight bring hurdles in childbearing [19, 20].In our study most of the females were having irregular menstrual cycle and the TVS showed that majority of the patient have immature small-sized follicles ranged from (0.5 cm to 1.2cm) which failed to achieve either ovulation or fertilization. It is reported that follicles those are either too small or too large are not considered as mature oocytes and also not suitable for fertilization [21]. According to the recent research it is very important that both the quality and quantity of oocytes should be perfectly measured before going to in vitro fertilization [22]. The (table 2) demonstrated that many of the infertile females were showing normal range of reproductive hormones according to the standard reference value, Sudha and Reddy have also the same opinion [23]. Present research gives evidence for that only (21.8%) of infertile females were showing hormonal disorder. In (Table 2) variables correlation results presents the considerable positive connection among FSH, LH, PROLACTIN and the age of observed patients, Lui with his colleague has given the similar statement in his research, that FSH concentration increase with increasing age, which confirms the ovarian dysfunction and female does not able to conceive [24]. It is reported that normal level of FSH is generally 3.5-12.5 mIU/ml, LH 2.4-12.6mIU/ml, Prolactin 71-348 mIU/ml, TSH 0.27-4.2µU/ml if level of these hormones drops down or rises than normal, it decreases pregnancy rates [25]. Hormonal balance has relation with food intakes, use of drugs and other factors like depression, workload due to these 70 females out of 127 facing irregular periods, 49 facing abnormal hair growths and 8 facing both of these problems [26]. In present study about 31 numbers of infertile females were showing the hormonal imbalance, 53 females were frequently eating chicken, 50 females were have normal workload and 46 females were receiving irregular menstrual cycle shown in table 1 and 2. According to tables (1, 2) there were no considerable connection among infertile female with their social surround and their residence, it can say that hormonal disorder does not only the reason of infertility, it is supposed as minor issue which can be cured by medicinal therapy this may indicate that these hormones do not interfere with those characteristics. Figure-2 shows that number of studied females were producing immature follicles as compared to there are less number of female who has mature oocytes. Previous research proved that the best quality of oocytes can be found in younger age

female, and these oocytes can be preserve for later age pregnancy [7].

CONCLUSION

In present findings, the maximum number of the studied women got immature follicles, which are unable to fertilize and become a reason of infertility; this may be due to chicken consumption and disturb eating and sleeping routine in their lives which causes hormonal imbalance for (LH, FSH, TSH and Prolactin). It is documented that FSH release raise with increasing age, as Prolactin concentration a little reduce with increasing age. Hence late marriages can be considered as another reason of infertility. Maintaining a healthy lifestyle, maintenance of normal body weight, early marriages and consuming healthy and proper diet can avoid childlessness. The remedial and social support of infertile women is essential to help in overcoming the problem. There are numbers of doors which can be knocked to cure female sterility such as medicines, minor surgery, laparoscopy, hormonal treatment.

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Data availability: data will be available on request

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

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AUTHORS' CONTRIBUTIONS: All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared.

REFERENCES

1. Sridevi, N. and M. Sandhya Rani, (2015) Study of thyroid profile in infertile women. IOSR J Pharm Biol Sci, 10(3): p. 57-61.
2. Pasi, A. and M. Hanchate, (2011) Infertility and domestic violence: Cause, consequence and management in Indian scenario.
3. Al-Fahham, A.A. and H.Q. Al-Nowainy, (2016) The Role of FSH, LH, and Prolactin Hormones in Female Infertility. International Journal of PharmTech Research, 6: p. 110-118.
4. Mahesan, A.M., et al., (2019) Knowledge and attitudes regarding elective oocyte cryopreservation in undergraduate and medical students. Fertility research and practice, 5(1): p. 5.
5. Giudice, L. and L. Kao, (2004) Endometriosis and Infertility. Lancet, 364(9447): p. 789-799.
6. Shirasawa, H. and Y. Terada, (2017) In vitro maturation of human immature oocytes for fertility preservation and research material. Reproductive Medicine and Biology, 16(3): p. 258-267.
7. Imani, B., et al., (1999) Predictors of chances to conceive in ovulatory patients during clomiphene citrate induction of ovulation in normogonadotropic oligoamenorrheic infertility. The Journal of Clinical Endocrinology & Metabolism, 84(5): p. 1617-1622.
8. Kanagavalli, P., et al., Lakshmi K,". (2013) A Study to assess the Hormonal Profile of Polycystic Ovarian Syndrome in a Tertiary Care Hospital in Puducherry", RJPBCS, 4(2): p. 1223-1228.
9. Karavani, G., et al., (2019) In vitro maturation rates in young premenarche patients. Fertility and sterility, 112(2): p. 315-322.
10. Kumar, D., (2007) Prevalence of female infertility and its socio-economic factors in tribal communities of Central India.
11. Lee, D.S., et al., (2013) Basal luteinizing hormone and follicular stimulating hormone: is it sufficient for the diagnosis of precocious puberty in girls? Annals of Pediatric Endocrinology & Metabolism, 18(4): p. 196.
12. Liu, X.M., et al., (2015) FSH regulates fat accumulation and redistribution in aging through the Gαi/Ca2+/CREB pathway. Aging cell, 14(3): p. 409-420.
13. Maman, E., et al., (2011) Luteal phase oocyte retrieval and in vitro maturation is an optional procedure for urgent fertility preservation. Fertility and sterility, 95(1): p. 64-67.
14. Mokhtar, S., et al., (2006) Risk factors for primary and secondary female infertility in Alexandria: a hospital-based case-control study. J Med Res Inst, 27: p. 251-61.
15. Nam, H.-K., et al., (2012) Factors to predict positive results of gonadotropin releasing hormone stimulation test in girls with suspected precocious puberty. Journal of Korean Medical Science, 27(2): p. 194-199.
16. Narjes D., T.M.d., Meimanat H. (2017) A Systematic Infertility-Related Risk Factors:. Review International Journal

of Women's Health and Reproduction science, (5): p. 24-29.
17. Patra, S. and S. Unisa, (2007) Female infertility in India: Causes, treatment and impairment of fertility in selected districts with high prevalence. Indicators, p. 08.
18. Revelli, A., et al., (2014) A critical review of bi-dimensional and three-dimensional ultrasound techniques to monitor follicle growth: do they help improving IVF outcome? Reproductive Biology and Endocrinology, 12(1): p. 107.
19. Roupa, Z., et al., (2009) Causes of Infertility in Women at Reproductive Age. Health science journal, 3(2).
20. Naveed, S., S. Ghayas, and A. Hameed (2015) Hormonal imbalance and its causes in young females. Journal of Innovations in Pharmaceuticals and Biological Sciences (JIPBS), 2(1): p. 12-16.
21. Anwar, S. and A. Anwar (2016) Infertility: A review on causes, treatment and management. Womens Health Gynecol, 5: p. 2-5.
22. Shakya, K. and B. Gubhaju (2016) Factors contributing to fertility decline in Nepal. Journal of Population and Social Studies [JPSS], 24(1): p. 13-29.
23. Roy, S. and S.M.I. Hossain (2017) Fertility differential of women in Bangladesh demographic and health survey 2014. Fertility research and practice, 3(1): p. 16.
24. Sudha, G. and K. Reddy (2013) Causes of female infertility: a crosssectional study. International Journal of Latest Research in Science and Technology, 2(6): p. 119-123.
25. Olooto, W.E., A.A. Amballi, and T.A. Banjo (2012) A review of Female Infertility; important etiological factors and management. J Microbiol Biotech Res, 2(3): p. 379-385.
26. Westoff, C.F., K. Bietsch, and D. Koffman (2013) Indicators of trends in fertility in sub-Saharan Africa. DHS analytical studies, (34).