Population Attributable Fractions of Caffeine and Water Pipe on Low Birth Weight: A Population-Based Prospective Cohort Study in Iran

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Abstract

Background

To estimate Population Attributable Fractions (PAFs) and Generalized Impact Fractions (GIFs) for LBW following scenarios to remove or decrease prenatal use of caffeine or water pipe.

Methods

Using data of 861 pregnant women from a population-based prospective cohort study in suburbs of Bandar Abbas city (2016-2018), PAFs and GIFs were calculated based on the relative risk scale. Practical interventional scenarios to reduce the exposure prevalence were developed for calculation of GIFs.

Results

The cumulative incidence of LBW was 16.1%. An estimated 19% (95%CI: 6, 30%) of LBW neonates was attributed to dietary caffeine intake of ≥100 mg/day and 11% (95%CI: 8,14%) to water pipe smoking. Action plans to reduce caffeine intake and water pipe smoking suggested an avoidable burden of LBW cases of approximately 10.7% (95% CI: 6.6, 25.3%) and 5.7% (95%CI: 5.0, 6.8%), respectively.

Conclusions

Water pipe smoking and excessive consumption of caffeine during pregnancy decreased birth weight. Practical action plans to control water pipe smoking and to prevent excessive intake of caffeine among pregnant women would substantially reduce LBW burden in the south of Iran.

Plain English Summary

This study followed 861 pregnant women residing in suburban areas until delivery. We were looking for the possible effects of water pipe smoking and excess caffeine intake by mothers on their baby $shea < h. Ourstudyshowedt\hat{w}ater\pi pesmok \in gatanytrimester \in pregnancycanbeariskfac \to rf \text{ or } \in fant$ s low birth weight. Furthermore, our data showed that pregnant women who consumed more than 100 mg/day caffeine (equal to two cups of black tea or one cup of brewed black coffee) were more likely to deliver a low birth weight infant. Finally, using statistical analysis methods, we showed the magnitude of decrease in low birth weight infants if A) we can prevent water pipe smoking from all the smoker women, B)we can prevent all pregnant women from excessive intake of dietary caffeine.

Introduction

Low Birth Weight (LBW), defined as the birthweight below 2500 grams, is associated with increased morbidities and mortalities in neonates (1). Previous studies have shown that 5.0 to 8.0% of Iranian neonates were born with LBW each year while our previous study on the same study setting showed that nearly 12% of the pregnancies resulted in LBW infants (2). LBW, a consequence of inadequate fetal weight gain in utero, has been linked to a variety of interrelated risk factors, amongst them tobacco smoking and dietary indulgence in caffeine intake (3-5). Due to the causative effect of cigarette smoking on LBW, concern has been raised to possible effect of other types of tobacco consumption such as water pipe (6). The results of the latest STEPS survey in Iran showed that water pipe is a prevailed mode of smoking in the south of Iran, where women used it more frequently than the rest of the country (7). Detrimental effects of water pipe smoking on pregnancy outcomes have been reported previously (2, 5, 8). LBW is also linked to the excess intake of

 e has not been fully worked out (9-11). From the

epidemiological point of view, the Population Attributable Fraction (PAF), defined as the fraction of all cases of a particular health condition that is attributable to a specific exposure, is an epidemiologic measure widely used to assess the public health impact of various exposures (12). However, interpretation of PAF relies heavily on interventions that can perfectly remove the exposure of interest. In other words, PAF interprets poorly for interventions for which success rate is below 100%. To overcome this conceptual pitfall, Generalized Impact Fraction (GIF), which calculates the change in the disease burden when a risk factor is altered, has been used by epidemiologists. While PAF simply studies complete elimination of a risk factor, GIF estimates the proportional reduction in disease incidence given a graded reduction in the prevalence of a risk factor (13). To the best of our knowledge, there is no epidemiologic evidence on the impact of designed interventions to prevent LBW by eliminating or reducing the level of caffeine intake and water pipe in Iran. Therefore, using data from a population-based prospective cohort study, the present paper estimated the anticipated incidence of LBW following interventions to reduce or eliminate the level of caffeine intake and water pipe.

Materials And Methods

The present study used data from the first two phases of a prospective cohort study entitled “A population-based prospective cohort study to identify contributors of mother and child health in suburban communities” in Bandar Abbas city, which is abbreviated as Bandar Abbas Pregnancy Cohort (BAPC). The study protocol was ethically approved and financially granted by the National Institute for Medical Research Development (NIMAD) with the approval code of 943607 and ethical code of N. IR.NIMAD.REC.1396.205. Since 2014, BAPC investigates the effects of lifestyle and environmental factors on child wellbeing and growth in Bandar Abbas city, the capital of Hormozgan Province in the south of Iran. The BAPC was designed to recruit and follow-up 1,000 pregnant women through door-by-door inquiry. Inclusion criteria defined as ages between 16-50 years, being pregnant, and being resident of the three most socially and economically vulnerable neighborhoods of Bandar Abbas. Exclusion criteria defined as inability to communicate in Farsi, unwillingness to participate or migration from the study area. Following a signed informed consent form, data from the subjects and their babies are gathering through four visits in pregnancy, 1, 6, and 12 months after birth. The details of the cohort methodology have been published elsewhere(14).

The present paper used the data of 897 subjects who completed the second visit of the BAPC (participation rate: 92%, response rate: 95.42%) during September 2016 to May 2018. The second visit was conducted during post-partum period (0-42 days post-delivery) by a visit to the mother$shome \text{ or } byte \leq pho \neq \int erviewbasedonthe \subset ject$s preference. The following cohort subjects were further excluded from the present analysis: pregnancies that ended up with miscarriage (n=24, 2.55%), stillbirth or multiple pregnancies (n=8, 0.85%), and pregnant subjects with self-reported cigarette smoking during pregnancy (n=4, 0.44%). Therefore, data of 861 live singleton pregnancies (mean ±SD gestational age at recruitment: 22.62±9.66 weeks) was included in the analysis (Figure 1). The main outcome of the study was LBW, defined as birth weight below 2,500 grams (1). The main exposures were water pipe smoking and caffeine intake during pregnancy both were measured on the first phase of the BAPC. Water pipe smoking during pregnancy (Yes regular/Yes often/No) was measured by a checklist recommended by the WHO (15) and was merged into Yes/No answers. The checklist was validated by a group of healthcare professionals and epidemiologists while the reliability was checked on a subset of BAPC subjects (n=25, Cronbach`s alpha=0.78). The checklist also contained additional information on age at smoking initiation, smoking duration, and number of water pipe sessions per day, and Environmental Tobacco Smoking (ETS). Due to the unavailability of a standard checklist to measure dietary caffeine intake, Bunker categorization of caffeine content of beverages was used as a guideline(16). Accordingly, a checklist was designed and validated by a team of nutritionist, epidemiologist and gynecologist to measure dietary intake of caffeine. The checklist contained a set of questions on daily intake of any type of caffeinated beverages available in the local market (including black coffee, instant coffee, black tea, green tea, hot chocolate, soft drinks) and caffeinated

 hecked on a subset of BAPC subjects (n=15, Cronbach`s

alpha=0.64). The cumulative daily dose of caffeine was then dichotomized to normal (0-99 mg/day) and high ($\geq$100 mg/day) groups (17). Based on the recommendations to receive at least nine prenatal visits by the national guideline for pregnancy healthcare package, prenatal care visit was defined as number of prenatal visits to healthcare center and/or gynecologist office to receive care (regular/irregular). Monthly expenditure as a proxy of socio-economic status was defined as average monthly of usual expenses of household during the last six months on housing, food, clothing, and healthcare.

Confounder selection was based on the Change-In-Estimate (CIE) strategy. The CIE selects covariates on the basis of how much their control changes exposure effect estimates, i.e. amount of confounding by the covariate. CIE strategy is recommended over the classic significance testing of the covariate coefficient since 1970 (18). Suppose RR_a and RR_u denote the estimated risk ratio with and without adjustment for the covariate; then RR_a/RR_u is traditionally used to judge change importance. By this strategy, an "important covariate" was determined as whether the change in the exposure effect estimate from adjusting for the covariate falls outside an interval of practical equivalence; e.g., $0.91 < RR_a/RR_u < 1.1$ (which is the 10%-change rule for the risk ratio modified to be proportionally symmetric) (19). Based on the CIE strategy, duration of water pipe smoking, maternal education, intake of iron supplement, infant sex, preterm birth, history of LBW infant, and monthly expenditure were included in the final regression model. RR_a for the effects of the main exposures on LBW were calculated using Modified Poisson regression models (20). The *Miettinen* formula was applied to calculate PAFs for caffeine intake and water pipe smoking (12, 21). Accordingly, we estimated the PAF from the estimated RR_a derived from the modified Poisson regression model for the exposure of interest (water pipe smoking and caffeine intake, both as dichotomous variables). The prevalence of exposure among cases (p_c) was estimated as 22.3% for water pipe smoking and 67.63% for caffeine intake equal or more than 100 mg/day. The PAF finally estimated as: $PAF = p_c(1 - 1/RR)$(12).

GIFs were calculated using the following formula:

$$GIF = \frac{\sum_{i=1}^{n} PiRRi - \sum_{i=1}^{n} P_i{}'RR_i}{\sum_{i=1}^{n} P_i RR_i}$$

Where, P_i denoted the proportion of the population in exposure category *i* (fact) (8.59% for water pipe, 56.98% for high caffeine intake). P_i` denoted the proportion of the population in exposure category after an intervention or other change (counter fact). Therefore, $P_i$` for water pipe was set as 3% as the estimated national prevalence of water pipe. To set P^{i}` for caffeine intake, we used the recommended dose of 100 mg/day caffeine in pregnancy by the world health organization as the safe threshold; hence, we hypothesized that an effective intervention would successfully decrease the proportion of women with high intake of caffeine to 14.9%. Finally, RR_a denoted adjusted relative risk derived from the modified Poisson regression model (13). GIFs were calculated based on a series of proposed action plans for: a) decrease caffeine intake to less than 100 mg/day in subjects with excessive intake of caffeine; and b) decrease prevalence of water pipe smoking to the estimated national prevalence (i.e. 3% among 25-54 years old Iranian women(7)). All the analyses were performed using Stata version 13 (Stata Corp., College Station, TX, USA). P-values less than 0.05 were considered statistically significant for the final model.

Results

Out of 861 newborns, one hundred and thirty-nine (16.14%) were LBW, while the incidence of LBW was higher in illiterate/ elementary education group (21.1%), those with no prenatal intake of iron supplementation (19.3%), and those with a history of LBW newborn (24.5%). Overall, 482 (56%) of the pregnant women reported intake of more than 100 mg/day caffeine, among whom the three most frequently reported sources of caffeine were black tea (43.3%), soft drinks (33.8%), and instant coffee (19%). Compared to the group with normal caffeine intake, the proportion of LBW neonates was significantly higher in mothers with high caffeine intake during pregnancy (13.2% vs. 18.4%, p=0.038). Sixty-nine (8.59%) pregnant women reported water pipe smoking, with an average of 1.87 sessions per day. Compared to non-smokers, the proportion of LBW neonates was significantly higher in mothers who smoked water pipe during pregnancy (14.27% vs. 37.68%, $p \leq 0.001$). Additionally, the mean (SD) of water pipe smoking duration was 6.7 (30.8) months. The mean (SD) duration of water pipe smoking was significantly higher in mothers with LBW neonates (11.8 (43) vs. 5.8 (27) in normal-weight neonates, P=0.01) (Table-1). After adjustment on duration of water pipe smoking, maternal education, prenatal iron supplementation, infant sex, preterm birth, history of LBW infant, and monthly expenditure; intake of more than 100 mg/day caffeine during pregnancy increased the risk of LBW by 36% (RR_a=1.36, 95%CI:1.00,1.88). The risk of LBW was more than 2-times higher in women who smoked water pipe during pregnancy (RR_a=2.12, 95%CI: 1.32, 3.40) (Table-2). The results of PAFs showed that 19% (PAF=19%, 95%CI: 6.2, 30.3%) of LBW neonates would not have occurred if we could remove caffeine intake entirely during pregnancy. Moreover, 11% (PAF=11%, 95%CI: 8.3, 14.0%) of LBW neonates would not have occurred if we could successfully eliminate water pipe smoking from the population of pregnant women.

Furthermore, by implementing a community-based action plan to reduce the proportion of women with high intake of caffeine to 14.9%, 10.7% of LBW neonates would not have occurred (GIF=10.7, 95%CI: 6.6, 25.3%). Similarly, implementation of an action plan to reduce the prevalence of water pipe among pregnant women to the average national level (i.e. 3%) would decrease the number of LBW neonates by 5.7% (GIF= 5.7, 95%CI: 5.0, 6.8%). (Table 3)

Discussion

The present study used data of 861 live singleton births from the BAPC study. Sixteen percent of neonates were born with LBW while one-third of them were preterm as well. The incidence of LBW in our sample of suburban residents was higher than the estimate by the UNICEF (8%) and previous studies in Iran (5, 22, 23).

Overall, 73% of the study subjects reported consumption dietary caffeine on any dose during their current pregnancy while the average dose of caffeine was 104.7 mg/day. By defining the threshold for the safety dose of caffeine as 100 mg/day (17), we found that 56% of our study subjects reported excessive intake of caffeine. We also observed that women belonging to lower educational and socio-economic groups and those who used water pipe reported higher doses of caffeine intake. The estimated dose of caffeine intake in our study was similar to the reports from the US and Poland (24, 25). The primary sources of dietary caffeine in our study; however, disagreed with the reports from the developed countries. While black tea (60%) and soft drinks (44%) were the predominant sources of caffeine intake in our study, black coffee was the dominant source of caffeine intake in the developed world. This discrepancy can be attributed to social and cultural context. Differences in weather circumstances and availability and affordability of black tea and soft drinks advertise their consumption over other sources of caffeine (e.g. coffee or chocolate). Nevertheless, due to the lack of national estimates on the pattern of caffeine intake in Iran, we are unable to provide a valid comparison on caffeine consumption in our sample of pregnant women to the general population. Our study showed that consumption of more than 100 mg/day caffeine significantly increased the risk of LBW, which was consistent with the results of previous studies(10, 26). We used one-week dietary recall to measure daily intake of caffeine during pregnancy. Due to many exogenous and endogenous factors, it is likely that the measured dose of caffeine did not necessarily reflect the actual concentration of metabolites in the woman`s body (27). Moreover, we are aware that the

amount of caffeine in beverages is heavily determined by methods of beverage preparation; therefore, non-differential misclassification bias for the measured dose of caffeine is likely (9).

The self-reported prevalence of water pipe smoking during pregnancy was 8% among the study subjects, which was higher than previous estimates in Iran (7, 28); yet similar to the estimates from countries of Arabian Peninsula (29, 30).

Consistent with previous reports (31, 32), we found that water pipe smoking during pregnancy significantly increased the risk of LBW.

The final hypothesis of our study was the extent to which partial or complete removal of either exposures of interest would reduce the risk of LBW. To answer that, we calculated PAF, which is defined as the fraction of all cases of an adverse condition in a population that is attributable to a specific exposure (12). We estimated that 11% and 19% of LBW cases would be prevented if interventions to eliminate water pipe smoking or dietary caffeine intake were to be implemented, respectively. In order to interpret PAF using our observational data, we must assume that removal of the study exposures did not affect or alter the distribution of other risk factors for LBW (such as cigarette smoking instead of water pipe). We also must assume that there was no bias in the study design and data analysis, which means that the estimated effects were adjusted for all measured confounders (12). The estimate of PAF only applies to interventions that can successfully and completely remove the exposure of interest, while such successful interventions, especially in lifestyle factors, are scarce. For this reason and to calculate the impact of partially successful interventions, we developed real-time scenarios and calculated GIF, which measures the reduced fraction of cases that would result from changing the current level of the exposure to some modified level (13). The first intervention was designed to decrease the proportion of women with high intake of caffeine among pregnant women whose daily caffeine consumption was above that level. By doing so, 19% of LBW neonates would be prevented. The second scenario aimed to decrease the marginal prevalence of water pipe to the estimated national level of 3% among women. Implementation of such program would result in 11% reduction in LBW cases.

This study used data from a population-based sample to find the extent to which various preventive interventions on caffeine intake and water pipe smoking would influence the risk of LBW. Despite the high generalizability of population-based samples, our results should be translated carefully. We restricted our study subjects to women who had conception without medical assistance and had no history of infertility, hence our sample might be a healthier sample compared to the general population of women at reproductive age (33). Caution must be taken if the estimated effects of water pipe smoking and caffeine intake are to be generalized to women who had prior history of infertility or medically-assisted conception. Moreover, generalization of the estimated PAF requires similar distribution of the outcome as well as valid estimates for the exposure effects in the target population (12). The possible mediation effect of preterm birth in causal pathway between exposures of interest and LBW is another crucial note to keep in mind. Whether preterm birth lies in the causal pathway from water pipe or caffeine to LBW is not clear yet. Nonetheless, the likelihood of this association is acknowledged and we recommend caution in using the results of our study to preterm infants.

The present study was one of the first prospective epidemiologic studies to investigate public health impacts of caffeine and water pipe on reproductive outcomes in Iran. It used data from a prospective cohort project, while the suitability of prospective epidemiological studies to investigate pregnancy outcomes has been well-documented (33, 34).

Some limitations worth mentioning as well. We calculated the risk of LBW based on a risk set of total live births, whereas, the true theoretical risk set is defined as the total of successful conceptions. Therefore, the estimated risk of LBW might be inflated due to exclusion of unsuccessful pregnancies from the denominator (33). Furthermore, questionnaire-based data was used to estimate the prevalence of water pipe based on a systematic review done by *Akl*

 ubstance absorption following water pipe smoking is not

practical due to the lack of a ubiquitous standard tool. Therefore, the estimated magnitude and effects of water pipe on pregnancy outcomes might be different from previous results partly because of using various definitions and data collection tools. Additionally, we did not measure the chronic use of water pipe as an important predictor of fetal growth. This was because of the inconclusive evidence regarding such association at the time of the BAPC development. Therefore, our results only apply to water pipe use during pregnancy rather than continuous water pipe smoking.

Conclusions

Our study showed that water pipe smoking and excess consumption of dietary caffeine during pregnancy could decrease birth weight in deprived communities in the south of Iran. A notable proportion of LBW neonates can possibly be prevented by eliminating dietary caffeine and water pipe from pregnant women. Practical community-based action plans to control water pipe and to prevent excess intake of caffeine among pregnant women would substantially reduce LBW burden in the south of Iran.

Abbreviations

LBW: Low Birth Weight

BAPC: Bandar Abbas Pregnancy Cohort

STEPS survey: STEPwise approach to Surveillance

NIMAD: National Institute for Medical Research Development

ETS: Environmental Tobacco Smoking

WHO: World Health Organization

CIEstrategy: Change-In-Estimate strategy

RR_a: Relaive Risk Adjusted

RR_u: Relative Risk Unadjusted

PAF: Population Attributable Fraction

GIF: Generalized Impact Fraction

UNICEF: United Nations Children's Fund

Declarations

Ethics approval and consent to participate:

The ethical approval for the present study was granted by the National Institute for Medical Research Development (Code: N. IR.NIMAD.REC.1396.205) and by the institutional review board of Tehran University of Medical Sciences (Code: 42933244/3246). Verbal and written informed consent was sought from study subjects prior to interviews.

Consent for publication:

Not applicable

Availability of data and materials:

The data that support the findings of this study are available from the National Institute for Medical Research Development but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the National Institute for Medical Research Development.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

S.N: Conceptualization, Design of the work, Original draft

M.A.M: Design of the work, interpretation of data, Original draft

K. H: Conceptualization, drafting and revising the draft

A.R.F: Data analysis, interpretation of data, manuscript approval,

A.M.: Project administration, Funding acquisition, Validation

H.S.: Investigation, Project administration

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Tables

Table 1- General characteristics of BAPC subjects according to birth weight, 2016-18

Variable	Category	Total (%)	Birth weight, N (%)		P
			≥2500 g	<2500 g	
Caffeine consumption					
Caffeine intake (mg/day)	0-99	379 (44.02)	334 (86.75)	51 (13.25)	0.038
	≥100	482 (56.98)	388 (81.51)	88 (18.49)	
Pattern of water pipe smoking					
Water pipe smoking	No	792 (91.41)	679 (85.73)	113 (14.27)	<0.001
	Yes	69 (8.59)	43 (62.32)	26 (37.68)	
Duration of water pipe smoking (months)		6.77 (30.87)	5.80 (27.57)	11.82 (43.98)	0.0175
Maternal characteristics					
Age	≤30	563 (65.39)	477 (84.7)	86 (15.3)	0.341
	>30	298 (34.61)	245 (82.2)	53 (17.8)	
Occupation	Housekeeper	837 (97.21)	700 (83.6)	137 (16.4)	0.756
	Employed	24 (2.79)	22 (91.6)	2 (8.4)	
Education	Illiterate/elementary	241 (27.99)	190 (78.8)	51 (21.16)	0.038
	Middle/High school	494 (57.38)	426 (86.23)	68 (13.77)	
	Academic	126 (14.63)	106 (84.13)	20 (15.87)	
LBW history	No	739 (85.83)	630 (85.25)	109 (14.75)	0.006
	Yes	122 (14.17)	92 (75.41)	30 (24.59)	
Miscarriage history	No	837 (97.21)	702 (83.87)	135 (16.13)	0.944
	Yes	24 (2.79)	20 (83.33)	4 (16.67)	
Prenatal care visit	Regular	702 (81.53)	593 (84.47)	109 (15.53)	0.301
	Irregular	159 (18.47)	129 (81.13)	30 (18.87)	
ETS	No	637 (73.98)	543 (86.05)	88 (13.95)	0.733
	Yes	224 (26.01)	136 (85)	24 (15)	
Prenatal Iron supplementation	No	259 (30.08)	209 (80.69)	50 (19.31)	0.008
	Yes	602 (69.92)	513 (85.22)	89 (14.78)	
Prenatal vitamin supplementation	No	251 (29.15)	206 (82.07)	45 (17.93)	0.361
	Yes	610 (70.85)	516 (84.59)	94 (15.41)	
Monthly expenditure[£] (Mean ±SD)		6.18 (5.94)	6.29 (6.02)	5.60 (5.52)	0.041
Infant characteristics					
Infant sex	Boy	441 (53.26)	380 (86.17)	61 (13.83)	0.062
	Girl	387 (46.74)	315 (81.40)	72 (18.60)	

Preterm birth	No	801 (93.03)	704 (87.89)	97 (12.11)	<0.001
	Yes	60 (6.97)	18 (30.00)	42 (70.00)	
Birth order	1	351 (40.77)	290 (82.62)	61 (17.38)	0.414
	>1	510 (59.23)	432 (84.71)	78 (15.29)	

Environmental Tobacco Smoking (among non-water pipe smokers, n=792), [£] In 1,000,000 Iranian Rials

Table 2. Univariate and multivariate Modified Poisson Regression Models on low birth weight in BAPC, 2016-18						
Predictor	Univariate Poisson model			Multivariate Poisson model		
	β (Robust $SE_{(\beta)}$)	Risk Ratio (95%CI)	P	β (Robust $SE_{(\beta)}$)	Risk Ratio (95%CI)	P
Caffeine intake (mg/day)						
0-99	Reference			Reference		
≥100	0.49 (0.16)	1.64 (1.18,2.28)	0.003	0.31 (0.16)	1.36 (1.00,1.88)	0.055
Water-pipe smoking						
No	Reference			Reference		
Yes	1.11 (0.16)	3.05 (2.21,4.20)	<0.001	0.75 (0.24)	2.12 (1.32,3.40)	0.002
Water pipe smoking* Caffeine >$100_{mg/d}$	-	-	-	0.17 (0.35)	1.19 (0.59, 2.38)	0.201
Duration of water pipe smoking (months)	0.003 (0.001)	1.00 (1.000,1.007)	0.022	-0.003 (0.002)	0.99 (0.99,1.00)	0.261
Maternal education						
Illiterate	Reference			Reference		
Below diploma	-0.43 (0.16)	0.65 (0.46, 0.90)	0.010	-0.31 (0.15)	0.72 (0.53 ,0.99)	0.047
University degree	-0.28 (0.23)	0.75 (0.46,1.20)	0.231	-0.12 (0.24)	0.88 (0.55, 1.41)	0.608
Prenatal Iron supplementation						
No	Reference			Reference		
Yes	-0.13 (0.08)	0.87 (0.74,1.02)	0.096	-0.07 (0.07)	0.93 (0.79, 1.08)	0.349
Infant sex						
Boy	Reference			Reference		
Girl	0.29 (0.15)	1.34 (0.98,1.83)	0.063	0.25 (0.14)	1.29 (0.96,1.73)	0.081
Preterm birth						

No	Reference			Reference		
Yes	1.75 (0.12)	5.78 (4.50,7.41)	<0.001	1.56 (0.15)	4.78 (3.54, 6.44)	<0.001
History of LBW infant						
No	Reference			Reference		
Yes	0.51 (0.18)	1.66 (1.16, 2.38)	0.005	0.17 (0.18)	1.19 (0.83, 1.70)	0.332
Monthly expenditure*	-0.01 (0.01)	0.98 (0.95, 1.00)	0.107	-0.02 (0.01)	0.98 (0.95, 1.00)	0.178
Maternal age						
<30	Reference			Excluded		
>30	0.15 (0.15)	1.16 (0.85,1.59)	0.340			
ETS						
No	Reference			Excluded		
Yes	-0.08 (0.20)	0.91 (0.60,1.37)	0.079			
Birth order						
1	Reference			Excluded		
>1	-0.12 (0.15)	0.88 (0.64, 1.19)	0.414			
Prenatal care visit						
Irregular	Reference			Excluded		
Regular	-0.19 (0.18)	0.82 (0.57, 1.18)	0.296			

*in 1,000,000 Iranian Rials

Table 3- Population Attributable Fractions and Generalized Impact Fractions of caffeine consumption and water-pipe on the incidence of low birth weight			
Measure	Intervention	Estimate	95%CI
Population Attributable Fraction (PAF)	Caffeine	0.19	0.062, 0.303
	Water pipe smoking	0.11	0.083, 0.140
Generalized Impact Fraction (GIF)	Caffeine [A]	10.77	6.63,25.34
	Water pipe smoking [B]	5.72	5.02, 6.86

A:Intervention to reduce caffeine intake to 100 mg/d

B:Intervention to reduce the prevalence of water pipe smoking to 3%

Figures

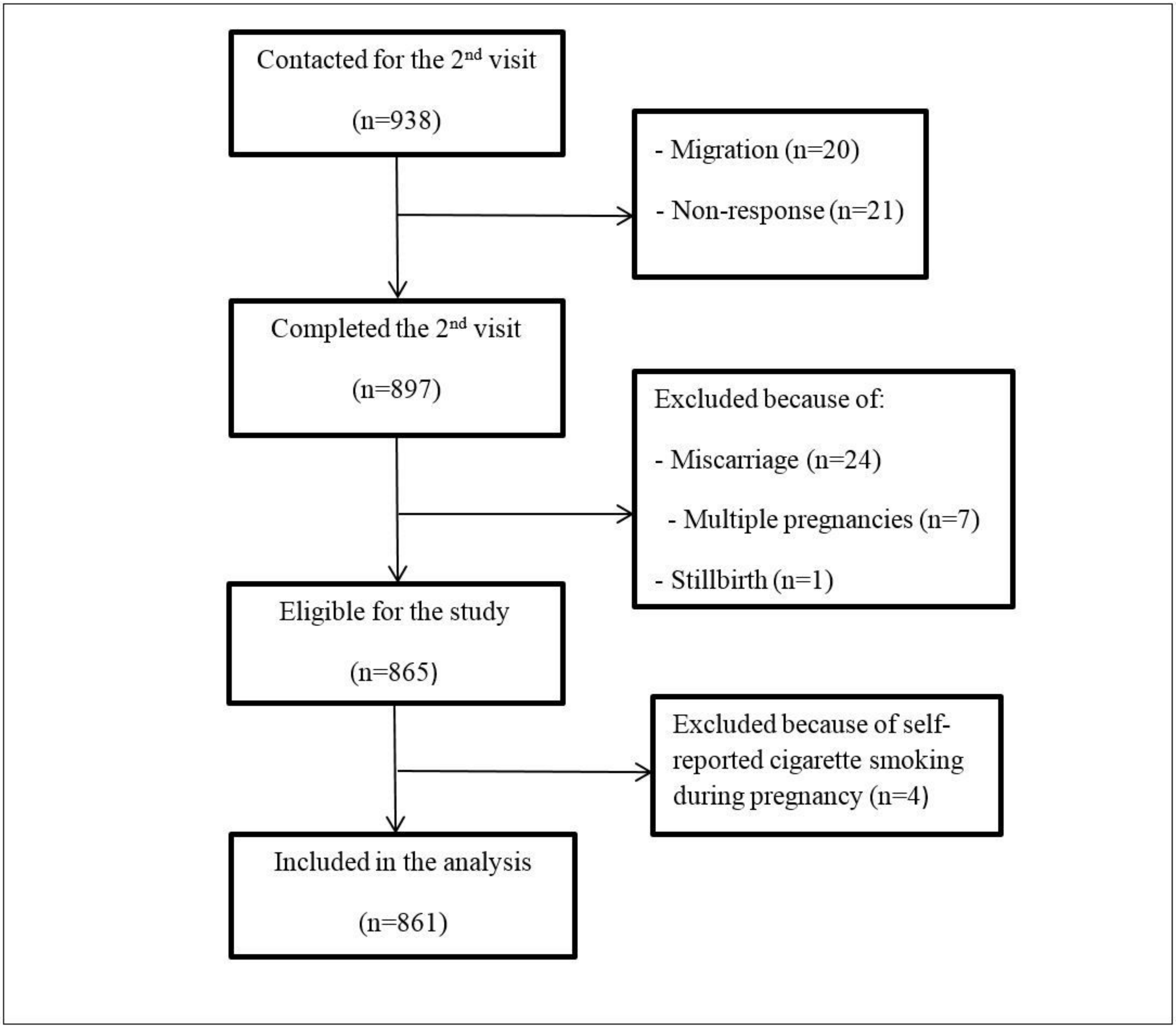

Figure 1

Flowchart of the BAPC subjects participated in the resent study

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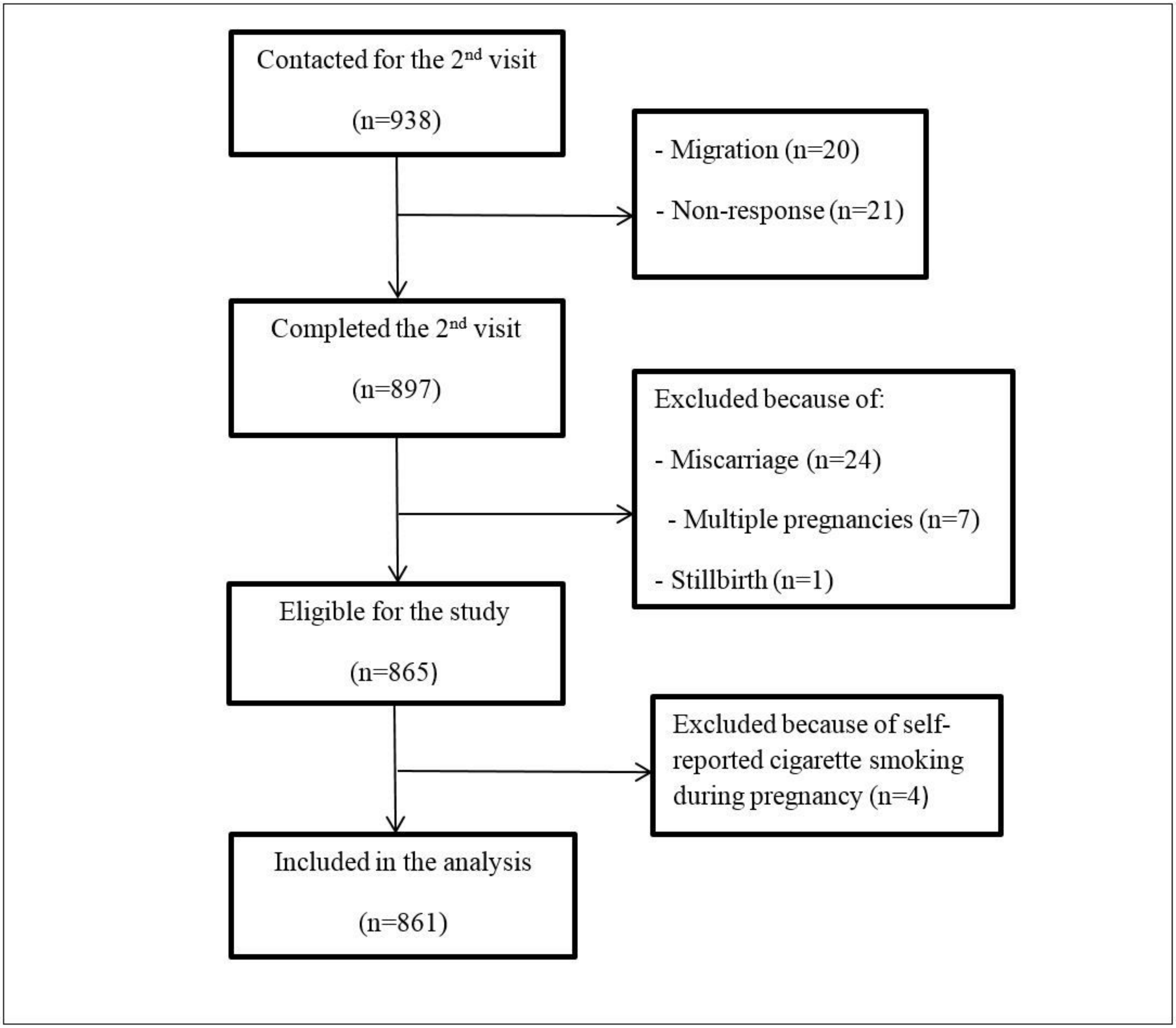

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